American Journal of Obstetrics and Gynecology

VOL. XXIV ST. LOUIS, DECEMBER, 1932 NO. 6

Original Communications

THE RELATION OF PLACENTAL INFARCTS TO ECLAMPTIC TOXEMIA*

A CLINICAL, PATHOLOGIC, AND EXPERIMENTAL STUDY

R. A. BARTHOLOMEW, M.D., AND R. R. KRACKE, M.D., ATLANTA, GA.

(From the Departments of Obstetrics and Pathology, respectively, Emory University School of Medicine)

ROUTINE inspection of the placenta, on surface and on section, has impressed us with the fact that there is a close relation between the occurrence of placental infarcts and eclamptic toxemia.

The fact that infarcts occur more frequently in the placentas of toxemic patients has been recognized for some time. According to Williams, Fehling, in 1886, was apparently the first to call attention to the connection between albuminuria of pregnancy and placental infarction. Following this, and up to the time of Williams' article in 1900, there appeared reports of similar series of cases by Rouhaud, Cohn, Rossier, Cagny and Martin, in which the frequency of placental infarcts in cases of albuminuria varied from 33 to 85 per cent. Williams, in an examination of 500 placentas, found infarcts of all types present in 63 per cent, but analyzed the lesions from the standpoint of the etiology and the types and not according to their relation to toxemia.

Young, in 1914, stimulated a renewed interest in the relation of placental infarcts to toxemia, by his description of the earliest stages of infarct formation. He traced the changes in the lesion from the dark, congested, purple or almost black appearance in the early stage, to a lighter brick-red or brown color as the lesion became older, and then to a yellow and gray-white color in the final stage. He emphasized that the placenta from a fulminating type of eclampsia may show no other lesions than one or more dark, congested or purple-black areas in the substance. He obtained experimental support to his theory by injecting extract from artificially autolyzed placenta, subcutaneously, into guinea pigs and produced

*Read, by invitation, at the meeting of the American Gynecological Society, May 31 to June 2, 1932, Quebec, Canada.

For lack of space it is not possible to print this paper in its entirety, but the complete paper may be had in the authors' reprints as well as in the current volume (1932) of the Society's Transactions.

muscular spasms, convulsions and death after several or more injections. Necropsy showed pathologic changes in the liver and kidneys very similar to those found in eclampsia.

* * * *

MATERIAL AND METHODS OF AUTHORS' INVESTIGATIONS

In order to follow up the suggestive clinical evidence of a relation between placental infarcts and eclamptic toxemia, the placentas from all deliveries from seven months on to full term were fixed from one to several weeks in 10 per cent formalin. Among these were occasional placentas from abortions of five or six months which were examined but not included in the series. The material was obtained from the obstetric services of Emory University Hospital (white) and Grady Hospital (colored). In each case the clinical record was obtained and notation made as to hemorrhage and particularly as to evidence of toxemia during pregnancy. The diagnosis of toxemia during pregnancy was based principally on albuminuria and a blood pressure in excess of 135 systolic and 85 diastolic, taken in conjunction with the usual symptoms of toxemia. The incidence of such cases was relatively much higher on the colored service, probably due to inaccuracies in the histories given by the patients and the greater prevalence of hypertension and albuminuria among colored patients, due to infected teeth and tonsils.

The placentas were cut in strips about 1 cm. in width and all lesions 5 mm. or more in diameter, were described as to location, size, color, consistency and composition insofar as could be judged from the gross appearance. Specimens typical of the various types of lesions were saved in formalin for microscopic examination. The microscopic appearance of each type of lesion was correlated with the gross appearance and with the clinical record.

Experimental support of the theory that the autolysis of placental infarcts is responsible for eclamptic toxemia, was sought through injections of Berkefeld filtrate of artificially autolyzed normal placenta into rabbits and guinea pigs. To determine whether autolysis of other human tissues would produce similar effect, the autolysates of liver and kidney were used.

A total of 1000 placentas was examined, the specimens being saved in consecutive order, 327 being obtained from the white service (private) and 673 from the colored service (charity). It was necessary, first to classify the various lesions, and inasmuch as such a classification must be based on the etiologic factors concerned, it will, first of all, be necessary to state our own views as to the cause of the lesions commonly called placental infarcts.

AUTHORS' THEORY AS TO ETIOLOGY AND EFFECT OF PLACENTAL INFARCTION

It is unquestionably true that certain placental lesions result from a physiologic endarteritis which becomes more marked toward the end of

pregnancy, as emphasized by Ackermann, Eden, Williams and others. This is not only readily demonstrated microscopically but can be easily recognized on close examination of the fresh placenta. By stripping away the amnion on the fetal surface of the placenta, over the vessels

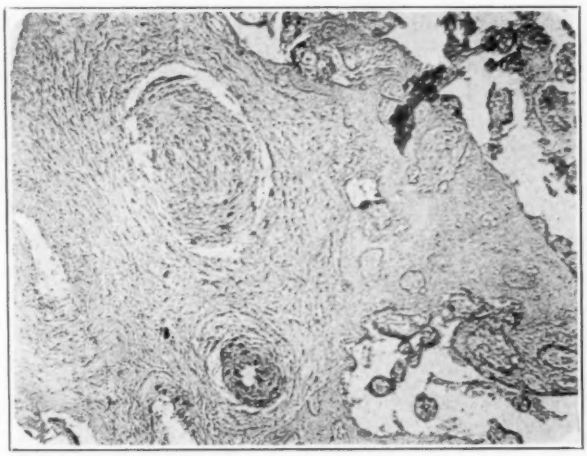


Fig. 1.—Complete occlusion of villous vessel from physiologic obliterative endarteritis.

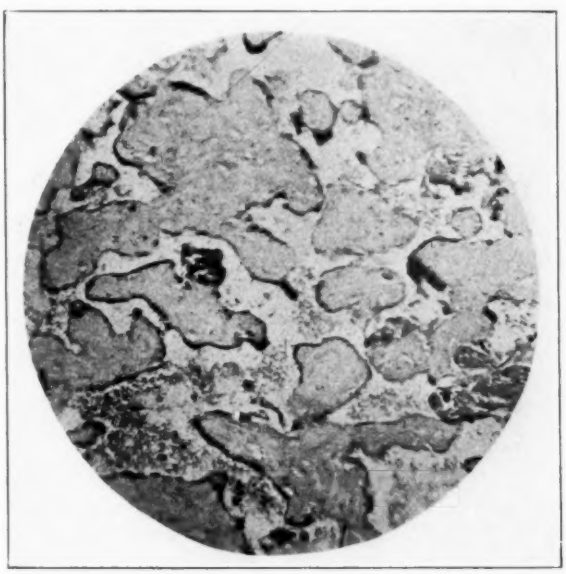


Fig. 2.—Hyalinization of villi resulting from very gradual obliterative endarteritis. Type 1 infarct, nontoxic.

leading to the infarcted area, one can usually demonstrate vessels which are entirely obliterated and appear as mere fibrous strands. Fig. 1 shows complete obliteration of a villous vessel. It is not at all difficult to find various degrees of partial obliteration of fetal vessels in sections from mature placentas.

The effect of this gradual shutting off of the circulation to the affected area is well described by Williams. There is a slow coagulation necrosis affecting the stroma and Langhans' layer, and later, the syncytium, which sets free products of necrosis, causing coagulation of maternal blood on the surface of the villi. In the early stages the nuclei are pyknotic but later on show karyorrhexis and karyolysis as a breaking up and finally a solution of the nuclear material takes place. If the circulation is diminished by very gradual stages, the entire villus and its branches, dependent on the affected vessel, apparently undergo hyaline change with formation of very little, if any, intervillous hyaline substance (Fig. 2). The absence of intervillous hyaline substance is probably accounted for by the extremely slight diffusion of products of

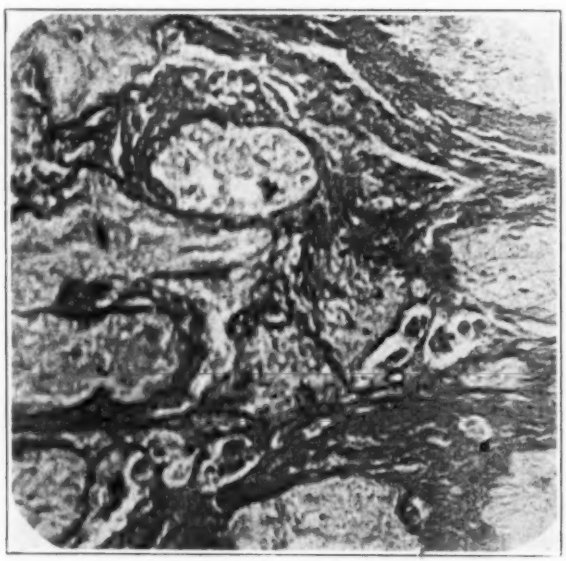


Fig. 3.—Pale "ghost villi" surrounded by dense hyaline intervillous substance resulting from obliterative endarteritis. Type 1 infarct, nontoxic.

necrosis, which do not reach sufficient concentration to cause coagulation of intervillous maternal blood. That hyalinization of the villi may progress without intervillous thrombosis is further favored by the fact that the syncytial layer which acts as an endothelium, is apparently more resistant to necrosis than the stroma or Langhans' layer.

If endarteritis proceeds somewhat more rapidly, the necrosis in the dependent villi is probably accelerated sufficiently to permit a more rapid diffusion of poisonous products and cause thrombosis in the intervillous spaces.

In this case, the coagulated maternal blood in the intervillous spaces takes on a hyaline appearance, the pale necrosed "ghost villi" becoming encased with deep staining homogeneous hyaline material in the early stages of necrosis of the villous stems, as shown in Fig. 3. Large masses

of villi are thus fused to form an infarct which derives its firm consistency and white appearance from the hyalinization and absence of circulation in the villi and intervillous spaces.

In this type of slowly developing infarct, we believe that the patient is protected against the poisonous products of autolysis of the placental protein by the fact that the gradual necrosis causes hyalinization of the villi or permits coagulation of maternal blood and formation of a protective zone of hyaline-like material around the villi, thus preventing the passage of poisonous products of villous disintegration into the maternal circulation. This accounts for the fact that firm, white infarcts may frequently be found in the placenta without any toxic manifestations.

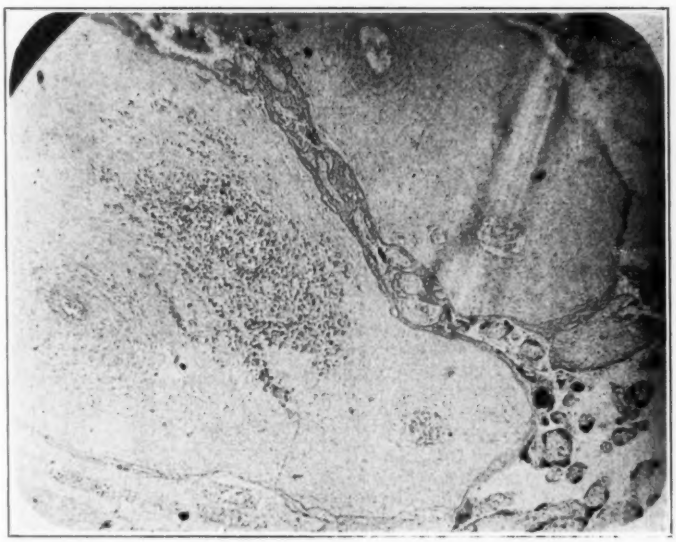


Fig. 4.—Extravasation of blood into stroma of villous stem, surrounding fetal vessel, probably due to trauma of fetal movements.

We believe there is another possible etiologic factor which may account for practically all other types of lesions. The trauma to which the fetal side of the placenta is subjected from the increasingly vigorous movements of the fetal extremities in the last two months of pregnancy must be taken into consideration. The force of these movements is considerable at times, as may be readily appreciated from palpation of the abdomen and from the evidence of pain shown by the patient. The placenta would probably receive more injury, were it not for the fact that it is usually situated on the anterior or posterior wall of the uterus, whereas, the natural position of the fetus is such that the fetal movements are usually directed to the right or left. If it is possible for a small superficial vein under the skin to be broken by a relatively slight trauma and result in an extravasation of blood in the tissues, it would

seem even more likely to occur on the fetal surface of the placenta, on account of the exposed and unprotected position of the fetal vessels. Furthermore, vessels which are undergoing endarteritic change would probably be more susceptible to injury.

At the site of the injury, thrombosis may occur with more or less rapid occlusion of the lumen, or a portion of such thrombus may easily become detached and occlude the main vessel or some of its branches. It is often possible to demonstrate a sudden diminution in the lumen of

Fig. 5.—Thick fibrin deposit beneath chorion on fetal surface of placenta, probably due to sudden rupture of fetal vessel from trauma of fetal movements.

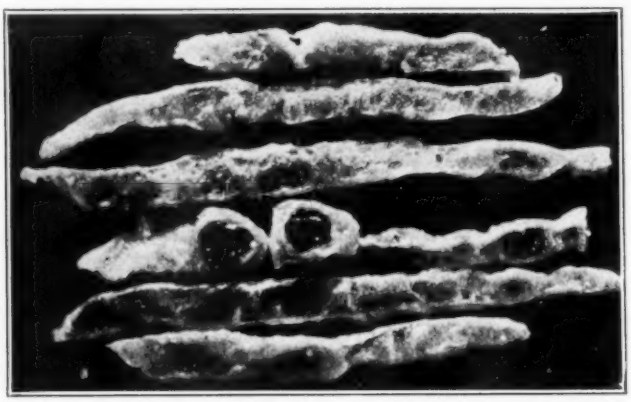


Fig. 6.—Cut strips of placenta from fulminating eclampsia, showing dark areas of early infarction and area of hemorrhage in substance of placenta.

a vessel by stripping the blood back toward the center of the placenta. On releasing the pressure, the width of the returning blood stream may be seen to diminish suddenly to a fraction of its former bed without any apparent cause, such as an anastomosis or division of the vessel.

Further evidence is offered by the appearance of the vessels shown in Fig. 4. Extravasation of blood into the walls of the vessels is distinctly shown, an appearance which could hardly be produced by any other cause than trauma. Actual rupture of a vessel on the fetal surface of the placenta from the trauma of fetal movements would produce a considerable extravasation of blood under the amnion or chorion and might well explain the appearance shown in Fig. 5. The thick layer of fibrin

represents a former collection of blood from which the hemoglobin has been absorbed. Such an appearance has usually been attributed to the very slow circulation of the maternal blood beneath the fetal surface which predisposes to coagulation and the deposition of fibrin. Since a sluggish maternal circulation in this location is common, to all placentas, it would seem reasonable to expect to find deposition of fibrin in practically all specimens, but such is not the case. Large deposits, as seen in Fig. 5, are comparatively rare. Small, localized deposits are occasionally seen. Furthermore, the same supposed factor must be present in placentas of four or five months but we know that such collections of fibrin are seldom, if ever, found at this stage, when the fetal movements and endarteritis are considerably less marked.

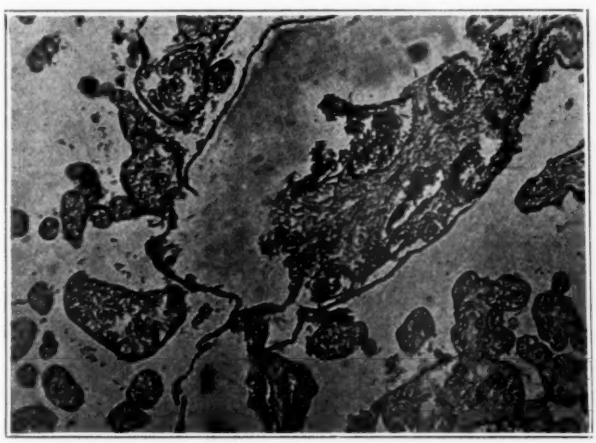


Fig. 7.—Photomicrograph from infarcts of placenta (Fig. 6), showing marked dilatation and rupture of villous capillaries and smaller vessels with acute necrosis of stroma, Langhans' layer and syncytium. Note absence of intervillous substance. Characteristic picture of preeclampsia and eclampsia.

If there is a sudden interruption in the circulation of a fetal vessel from rupture, thrombosis, or embolism, the area affected undergoes rapid degenerative changes. The gross appearance of acute lesions is shown in Fig. 6. The following is a brief history of the case:

S. R., colored, aged sixteen, primigravida; first prenatal visit seven months, November 18, 1931; blood pressure 104-68; no albumin; return visits November 25 and December 2; blood pressure not above 122-70; no albumin. Admitted to Grady Hospital January 22, 1932, false labor, blood pressure 120-86, apparently normal. Discharged January 23. Readmitted in coma, January 31, blood pressure 150-110, albumin 4-plus, many casts; severe headache preceding day; stupor and two convulsions just before admission. Treatment with glucose and magnesium sulphate intravenously. Labor induced by rupture of membranes. Normal delivery of living baby, weighing 2600 gm.; recovery.

The affected areas appear in the substance of the placenta as dark purple or almost black lesions in marked contrast to the surrounding normal red placental tissue. Coagulated or semifluid blood is seen in contact with some of these areas. The infarcted placental tissue still preserves its spongy, branching structure.

The microscopic appearance is shown in Fig. 7. A striking change is noticed in the appearance of the villous vessels and capillaries. They are markedly dilated and congested and some of the terminal capillaries are definitely ruptured, causing extravasation of fetal blood into the intervillous spaces. In some sections, both fetal

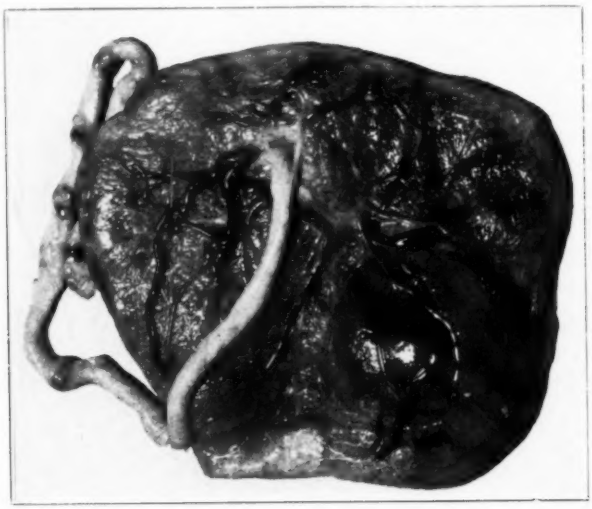


Fig. 8.—Placenta from fulminating eclampsia showing large subchorionic swelling due to hemorrhage under fetal surface of placenta, probably from trauma of fetal movements.

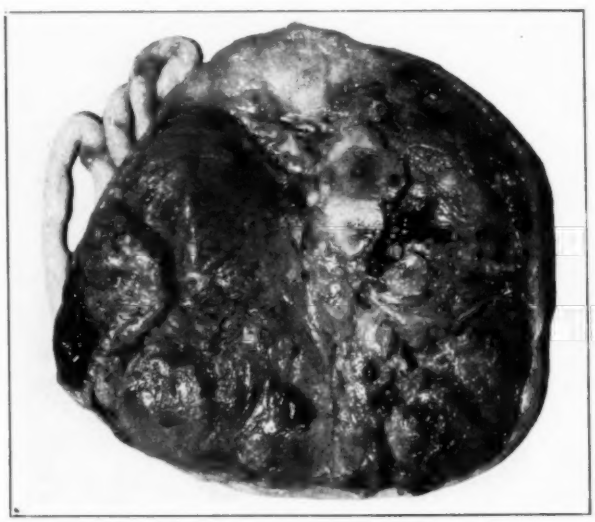


Fig. 9.—Rupture near center of maternal surface of placenta (Fig. 8) due to pressure of hemorrhage in substance of placenta.

and maternal blood cells can be seen in the intervillous spaces, due to a difference in the staining reaction. Thrombosis of some of the larger vessels may be seen. The stroma and Langhans' cells show early degenerative changes as evidenced by cloudy swelling, pyknosis and sometimes beginning disintegration. The syncytium appears to be more resistant, but pyknosis is usually evident in this layer also.

There is a striking absence of intervillous substance, and the maternal circulation between the villi is unobstructed. Consequently, the products of early autolysis, which are known to be exceedingly toxic, have free access to the maternal circulation.

The placenta from another case of fulminant eclampsia is shown in Figs. 8 and 9. The following is a brief history of the case:

Mrs. B., white, aged twenty-eight, primigravida, patient of Dr. A. S. Sanders; seen at office March 9, 1932, near end of seventh month, on account of headache.

Fig. 10.—Cut strips of placenta (Figs. 8 and 9) showing large brown infarcts in contact with main hemorrhage in substance of placenta. Lesion slightly older than those seen in Fig. 6.

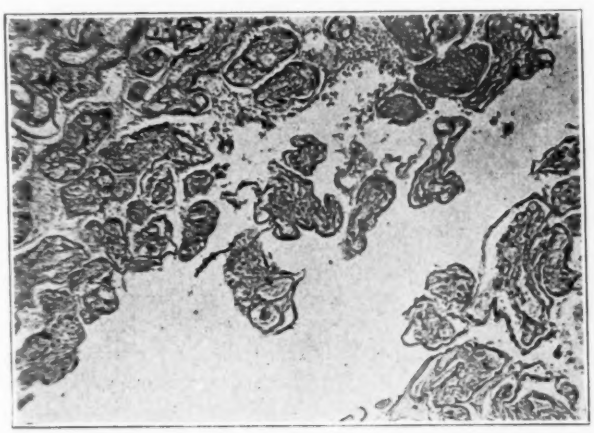


Fig. 11.—Photomicrograph from infarct shown in Fig. 10. Pathology same as shown in Fig. 7, except more advanced necrosis.

Blood pressure 125-80, slight trace of albumin. Restrictions of diet and exercise and increased catharsis advised. To return, March 14. Husband found patient unconscious on bathroom floor, 3 A.M. March 14. Three convulsions before admission to hospital. Blood pressure 140-90, albumin 4-plus, many casts. Labor induced by Voorhees bag. Normal delivery of living baby, weighing three pounds. Recovery.

There is a marked localized swelling about 8 cm. in diameter on the fetal side of the placenta. This is evidently due to sudden extravasation of blood from rup-

ture of a fairly large fetal vessel. The distention was sufficiently great to produce a star-shaped rupture of the placental tissue on the maternal surface. From the location and appearance of this hemorrhage, there is nothing to suggest its origin from rupture of a maternal vessel in the basal decidua or in a decidual septum between the cotyledons.

On section of the placenta, as shown in Fig. 10, several small, dark, spongy lesions are seen in the substance of the placenta, similar in appearance to those seen in Fig. 6, but the principal lesion is seen to be in contact with the area of hemorrhage, is more sharply defined and is of a dull chocolate brown color. The consistency is not spongy, but is more homogeneous and slightly firmer.

Microscopically, as shown in Fig. 11, different degrees of necrosis are seen, varying from pyknosis and cloudy swelling in the more recent spongy lesions, to extreme necrosis and disintegration with complete loss of staining power in the slightly older,

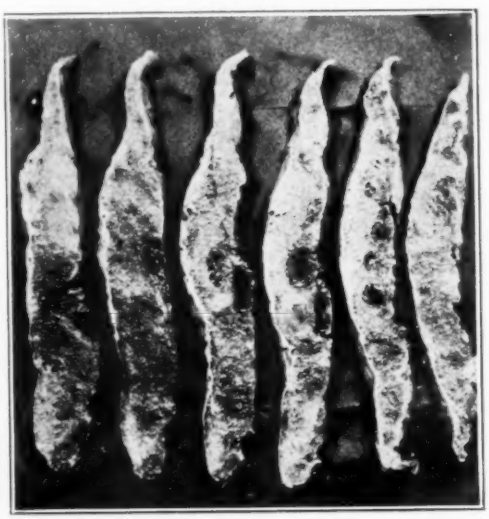


Fig. 12.—Cut strips of placenta from case of abruptio placentae showing infarcts exposed on maternal surface.

brown lesion. The villous capillaries are greatly dilated and congested. Many have ruptured. Thrombosis is seen in many of the larger vessels. There is practically no formation of intervillous hyaline substance. The color, demarcation, consistency and microscopic appearance mark the brown portion of the infarct as a slightly older lesion than in Fig. 6, and slightly more advanced in the process of disintegration and autolysis.

It is a well-known fact that abruptio placentae may occur, unexpectedly, in the course of preeclampsia and, conversely, that cases of abruptio placentae may unexpectedly develop eclampsia. Cases of abruptio placentae have been considered to be due to a toxin of a somewhat different nature than that causing eclampsia.

It has seemed to us that the process is essentially the same in both eclampsia and abruptio placentae and differs only in regard to the location of the infarct. If the lesion is in the substance of the placenta with intervening healthy placental tissue, separating it from the basal

decidua, the poisonous split-products of placental autolysis, of which histamine is probably one of the most active, are diffused through a wider intervillous circulation and are taken up by the decidual vessels of the entire placental site. In this case, the concentration of the poison is probably not sufficient to break down decidual sinuses and cause extravasation of blood with separation of the placenta. The pregnancy is therefore not interrupted at once and the general toxemia may reach such a degree that eclampsia occurs.

However, if the lesion is on the maternal surface, the concentration of the poisonous split-products of placental autolysis is brought to bear on the decidual sinuses in direct contact with the infarct and the effect, particularly of histamine, is probably sufficient to cause dilatation and

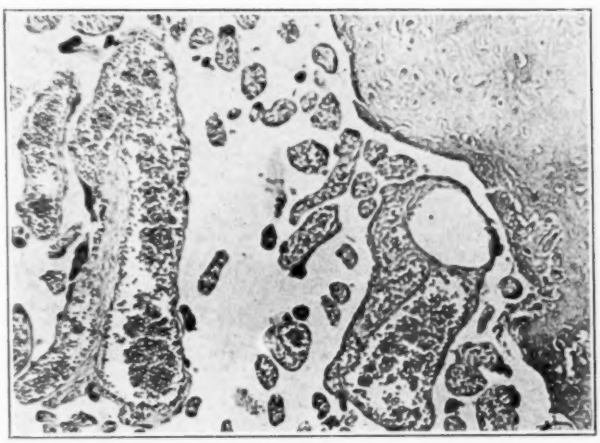


Fig. 13.—Photomicrograph from infarcts shown in Fig. 12. Pathology same as shown in eclamptic placentae.

rupture of the sinuses, extravasation of blood and separation of the placenta. In this case the pregnancy is usually interrupted before the general toxemia becomes marked enough to cause eclampsia. Since the infarction and the blood are of recent origin, the so-called "red infarct" has come to be recognized as a frequent accompaniment to abruptio placentae.

The appearance of such an infarct on the maternal surface of the placenta is shown in Fig. 12. The following is a brief history of the case:

Mrs. B., white, aged thirty-six, primigravida, patient of Dr. O. T. Malone, had an uneventful normal pregnancy until the sixth month. The blood pressure had not exceeded 115-70. Swelling of the feet began April 1, 1932, becoming generalized several days later. Severe headache and general malaise began April 8. Very little improvement from rest and other treatment. Marked increase in headache April 15. Severe cramp-like pains over lower abdomen, bleeding, nausea and vomiting, and marked dimness of vision April 16. Blood pressure 180-120. No convulsions. Spontaneous labor and delivery of stillborn, six months fetus. Large, firm clots ex-

ture of a fairly large fetal vessel. The distention was sufficiently great to produce a star-shaped rupture of the placental tissue on the maternal surface. From the location and appearance of this hemorrhage, there is nothing to suggest its origin from rupture of a maternal vessel in the basal decidua or in a decidual septum between the cotyledons.

On section of the placenta, as shown in Fig. 10, several small, dark, spongy lesions are seen in the substance of the placenta, similar in appearance to those seen in Fig. 6, but the principal lesion is seen to be in contact with the area of hemorrhage, is more sharply defined and is of a dull chocolate brown color. The consistency is not spongy, but is more homogeneous and slightly firmer.

Microscopically, as shown in Fig. 11, different degrees of necrosis are seen, varying from pyknosis and cloudy swelling in the more recent spongy lesions, to extreme necrosis and disintegration with complete loss of staining power in the slightly older,

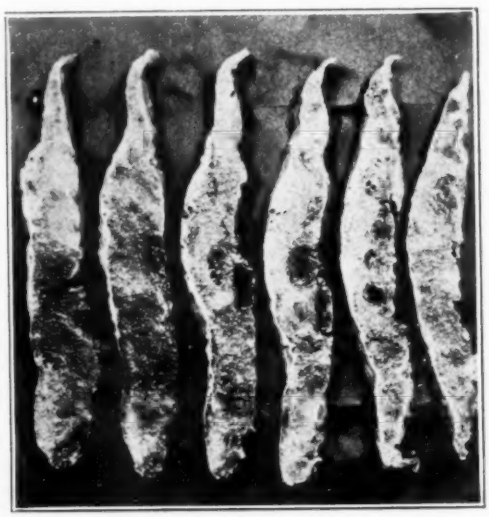


Fig. 12.—Cut strips of placenta from case of abruptio placentae showing infarcts exposed on maternal surface.

brown lesion. The villous capillaries are greatly dilated and congested. Many have ruptured. Thrombosis is seen in many of the larger vessels. There is practically no formation of intervillous hyaline substance. The color, demarcation, consistency and microscopic appearance mark the brown portion of the infarct as a slightly older lesion than in Fig. 6, and slightly more advanced in the process of disintegration and autolysis.

It is a well-known fact that abruptio placentae may occur, unexpectedly, in the course of preeclampsia and, conversely, that cases of abruptio placentae may unexpectedly develop eclampsia. Cases of abruptio placentae have been considered to be due to a toxin of a somewhat different nature than that causing eclampsia.

It has seemed to us that the process is essentially the same in both eclampsia and abruptio placentae and differs only in regard to the location of the infarct. If the lesion is in the substance of the placenta with intervening healthy placental tissue, separating it from the basal

decidua, the poisonous split-products of placental autolysis, of which histamine is probably one of the most active, are diffused through a wider intervillous circulation and are taken up by the decidual vessels of the entire placental site. In this case, the concentration of the poison is probably not sufficient to break down decidual sinuses and cause extravasation of blood with separation of the placenta. The pregnancy is therefore not interrupted at once and the general toxemia may reach such a degree that eclampsia occurs.

However, if the lesion is on the maternal surface, the concentration of the poisonous split-products of placental autolysis is brought to bear on the decidual sinuses in direct contact with the infarct and the effect, particularly of histamine, is probably sufficient to cause dilatation and

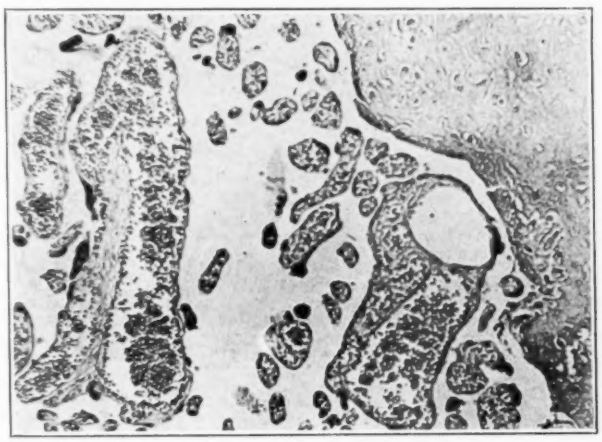


Fig. 13.—Photomicrograph from infarcts shown in Fig. 12. Pathology same as shown in eclamptic placentae.

rupture of the sinuses, extravasation of blood and separation of the placenta. In this case the pregnancy is usually interrupted before the general toxemia becomes marked enough to cause eclampsia. Since the infarction and the blood are of recent origin, the so-called "red infarct" has come to be recognized as a frequent accompaniment to abruptio placentae.

The appearance of such an infarct on the maternal surface of the placenta is shown in Fig. 12. The following is a brief history of the case:

Mrs. B., white, aged thirty-six, primigravida, patient of Dr. O. T. Malone, had an uneventful normal pregnancy until the sixth month. The blood pressure had not exceeded 115-70. Swelling of the feet began April 1, 1932, becoming generalized several days later. Severe headache and general malaise began April 8. Very little improvement from rest and other treatment. Marked increase in headache April 15. Severe cramp-like pains over lower abdomen, bleeding, nausea and vomiting, and marked dimness of vision April 16. Blood pressure 180-120. No convulsions. Spontaneous labor and delivery of stillborn, six months fetus. Large, firm clots ex-

pelled and placenta showed evidence of premature separation. Aching pain in region of liver April 19; numbness and weakness of left side. Blood pressure 150-100. Red blood cells in urine. Comatose condition April 20. Nonprotein nitrogen 173 mg. Urea 86 mg. Increased edema. Had five or six convulsions (uremic?). Died April 21. Necropsy. Brain convolutions flattened, suggesting increased pressure. No hemorrhage on surface. Liver showed numerous yellow areas on surface and section from few millimeters to several centimeters in diameter. Kidneys showed numerous hemorrhagic spots on stripping capsule. Marked engorgement. Microscopic examination: marked cloudy swelling, fatty degeneration, necrosis and scattered hemorrhages throughout liver lobules. Focal necroses with small round cell infiltration. Marked necrosis of renal epithelium, scattered hemorrhages, marked engorgement with free blood and numerous blood and hyaline casts. Glomeruli show marked engorgement and necrosis, acute hemorrhagic nephritis, and focal necrosis of liver.

The placental lesion is seen to be on the maternal surface. There has been some depression of the placenta in this region by the pressure of the clots which separated the placenta. The appearance of the lesion corresponds approximately to the dura-

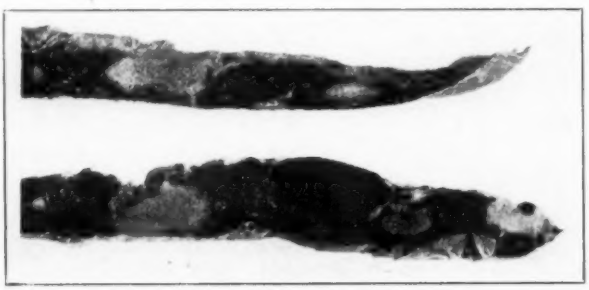


Fig. 14.—Strip of placenta from toxemia of three weeks' duration, terminating in eclampsia. Yellow, slightly softened infarct of subacute type near center and firm, white infarct from obliterative endarteritis on margin.

tion of the clinical symptoms, the affected tissue having a moderately firm consistency and light brown color.

Microscopically, as shown in Fig. 13, the villi show pyknosis, cloudy swelling and marked engorgement and dilatation of the capillaries in some areas; other villi show more advanced necrosis, disintegration and total loss of staining power, in the area bordering on the hemorrhage. The pathologic picture is the same as shown in Figs. 7 and 11, taken from the placental infarcts of the eclamptic cases.

Fulminating eclampsia and abruptio placentae do not occur as frequently as the gradually progressing type of toxemia of several weeks' duration, which eventually terminates in eclampsia, provided labor does not come on spontaneously or by artificial means. This type of toxemia is probably due to a more gradual or incomplete blockage of the circulation of a fetal vessel from thrombosis, possible rupture, embolism or even rapidly progressive endarteritis. By the time labor supervenes or is induced, the lesions have become yellow or dull gray and are well demarcated from the surrounding normal placenta. They lie mainly in the substance of the placenta but usually encroach to some extent on the maternal surface. Occasionally they may be situated on the edge

of the placenta, although in this location the lesion is usually of the nontoxic type and slow in development. Small succenturiate lobes are frequently the site of this type of infarct. There may be coagulated or semifluid blood, of a dull brick-red or brown color, in contact with the lesion. The consistency is homogeneous but only moderately firm and may yield scrapings to the knife.

The gross appearance of such a lesion is shown in Fig. 14. The following is a brief history of the case:

Mrs. B., white, aged twenty-four, primigravida, developed evidences of toxemia at the eighth month of pregnancy, with increasing edema, albuminuria, hypertension, and headaches. Within three to four weeks, blood pressure had increased to 170-110

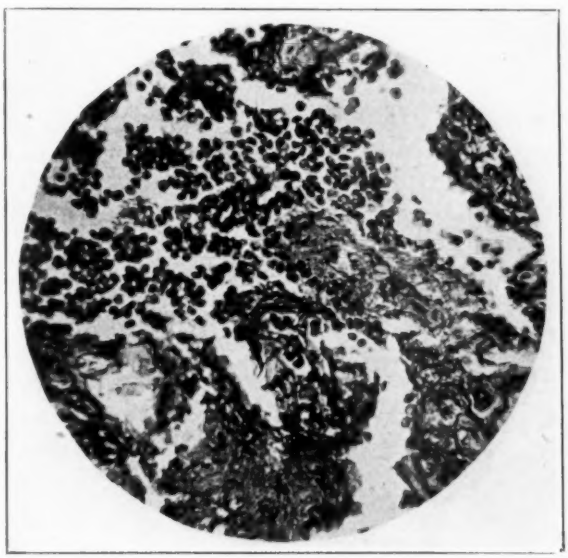


Fig. 15.—Photomicrograph of subacute infarct shown in Fig. 14. Marked necrosis of villi and absence of intervillous substance.

and albumin 3-plus. Labor induced on account of preeclampsia. One convulsion during labor. Normal delivery, living baby. Recovery.

Microscopically, the appearance is shown in Fig. 15. The nuclei have lost their staining power. There is marked disintegration of the stroma, Langhans' layer and even the syncytium. In this area of the infarct the necrosis has been more rapid, coagulation of the blood in the intervillous spaces has probably been inhibited by anticoagulant toxic products, and the diffusion of the products of autolysis into the general circulation eventually reached such a concentration that eclampsia finally occurred. It is not uncommon in the subacute or slightly older lesions to find some variation in the extent of formation of intervillous hyaline substance, intervillous maternal circulation and degree of degenerative change in different parts of the same lesion (Fig. 16). Such variations in the pathologic process may account for the variations sometimes shown in the clinical features during the course of preeclampsia, as, for example, unexplained variations in blood pressure and albuminuria; unexpected improvement or rapid change for the worse.

Due to the fact that the subacute type of infarct is apparently associated with a progressive toxemia which ultimately results in eclampsia after several weeks or necessitates induction of labor, the lesion may not reach a healed quiescent stage, such as is seen in the firm, white lesions on the edge of the placenta resulting from slow physiologic endarteritis.

In addition to the infarcts heretofore discussed, which are made up chiefly of villi and intervillous blood or hyaline substance, certain other lesions are found which merely represent localized hemorrhages. In those of recent origin, the blood may be semifluid or appear as a soft, black clot. The villi are forcibly pushed aside as the blood clot forms. In hemorrhages of longer standing, striations of fibrin in fan-like arrangement may be seen, and the color gradually becomes a lighter red or brick color as the red cells break down and the hemoglobin disappears. Eventually the fibrin alone remains, giving the lesion a yellow

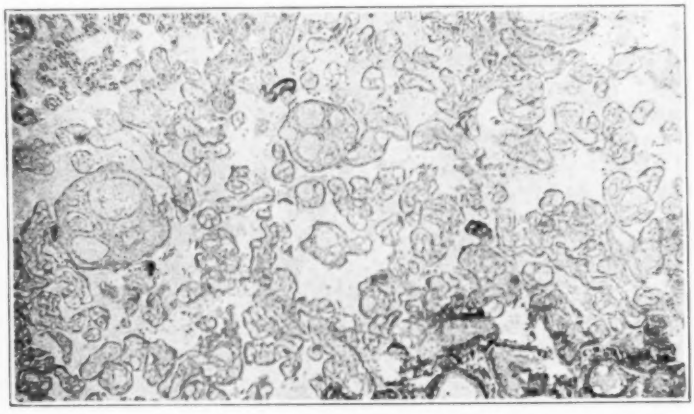


Fig. 16.—Photomicrograph from subacute placental infarct from case of moderately severe toxemia. Upper deep staining zone is oldest and shows partial formation of intervillous substance; light zone shows dilated, ruptured villous vessels, necrosis, thrombosis and open intervillous spaces; lower zone shows more recent involvement.

or gray white appearance. The consistency is rather soft and the fibrin can be broken away in flakes or layers.

Certain hemorrhagic areas seem to contain sufficient anticoagulant substance, such as peptone body, probably from some degree of necrosis of villi on the border of the area, to remain semifluid. Fibrin is absent or very limited, and through absorption of hemoglobin the contents become gelatinous or cystic. Complete absorption of the contents may possibly account for the open spaces occasionally seen in the placental substance, which Hartmann and Siddall have attributed to bacterial action after delivery.

A large proportion of the hemorrhagic and fibrinous areas is found under the fetal surface or in the placental substance. They are separated from the basal decidua by intervening healthy villi and normal intervillous maternal circulation. While it is difficult to prove the origin of these areas, we believe they arise either from traumatic

rupture of a main villous vessel or from the dilatation and rupture of the capillaries of the terminal villi, following traumatic thrombosis of this main vessel. It is difficult to explain their origin from rupture or obstruction of maternal vessels in the basal decidua or in the decidual septa. Our conception of the sinus-like circulation at the placental site and the unusually free communication between the villi, argues against the possibility of any portion of the placenta being entirely cut off from maternal blood.

* * * *

It is our belief, therefore, that all placental lesions, excepting some of the gelatinous areas, may be attributed to interference with the fetal circulation which may be brought about either in a gradual manner from physiologic endarteritis or in an abrupt manner from actual vascular rupture, thrombosis or embolism produced by the trauma of fetal movements.

The infarcts of acute or subacute development are probably responsible for eclampsia and abruptio placentae according to whether they are situated in the substance or on the maternal surface of the placenta. Infarcts of slow development are seldom if ever responsible for toxemia.

CLASSIFICATION AND FREQUENCY OF PLACENTAL LESIONS

The following description of the essential features of the lesions found in our own series corresponds closely to that given by Hartmann and Siddall in their own study:

Type 1.—Oval or round lesions, usually from one to several centimeters in diameter; white or pearly gray; of firm consistency; compact; nonstriated; usually situated near or on the border of the placenta and on the maternal surface; calcification may be present. Microscopically: pale necrosed villi fused by homogeneous deep staining hyaline intervillous substance. Villous vessels not dilated or ruptured.

This type of infarct is the result of physiologic endarteritis and is of no importance from the standpoint of eclampsia. It was found in 40 per cent of the white cases and 38 per cent of the colored.

Type 2.—Oval or round lesions, one to several centimeters in diameter; light pink, red, dark brown, or black; occasionally striated; usually situated in the placental substance. Microscopically: red blood cells and lamellae of fibrin; no villi.

This type of lesion is a true hemorrhage resulting from rupture of a fetal vessel or capillary, directly or indirectly from the trauma of fetal movements. It was found in 12.5 per cent of the white cases and 11.5 per cent of the colored. Toxemia will depend on the degree of secondary necrosis of villi dependent on the vessel or bordering on the hemorrhage.

Type 3.—Oval or round lesions, one to several centimeters in diameter, gray or white, occasionally slightly pink; striated or in lamellae, usually situated in the substance of the placenta but frequently under the fetal

surface. Microscopically: mainly fibrin layers; occasionally degenerated red cells; no villi.

This type is apparently a late or final stage of Type 2 lesion, in which the red cells have disintegrated and the hemoglobin has been absorbed. It was found in 5.5 per cent of the white cases and 6 per cent of the colored. Not primarily associated with toxemia.

Type 4.—Round or oval lesions, one to several centimeters in diameter, dark purple in the acute form, brown to yellow in the slightly older forms, soft and spongy in the acute stage but homogeneous and slightly firmer in the subacute stage; situated in the mid or outer zone of the placenta and usually in the substance or on the maternal surface of the placenta; lesion is often in contact with semifluid blood or clot. Microscopically: villi in various stages of necrosis, more advanced in brown or yellow lesions; villous capillaries and veins markedly dilated and distended in acute forms, less in subacute; occasionally ruptured; engorgement causes villi to appear more crowded; very little, if any, formation of hyaline intervillous substance. Thrombosis of villous vessels frequently seen.

This type is a true infarction resulting from rupture of a fetal vessel or occlusion from thrombosis or embolism, from the trauma of fetal movements and is probably the cause of abruptio placentae and eclamptic toxemia. It was found in 4.2 per cent of the white cases and 4.8 per cent of the colored.

Type 5.—Irregularly shaped, round or oval lesions somewhat smaller than the other lesions, transparent or slightly opalescent, occasionally slightly pink; some apparently encapsulated, others bordering directly on villi and always in placental substance. Microscopically: structureless, homogeneous material, occasionally surrounded by capsule of decidual cells; no villi. These lesions may represent degeneration of decidual septa; in other cases apparently the final stage of a hemorrhagic area in which fibrin formation was possibly inhibited by a peptone split-product. This type of lesion is of no clinical significance.

Although we agree with Hartmann and Siddall as to the essential features of the four types of lesions, there is a considerable difference of opinion as to the incidence of each type of lesion. In our own series we are certain we have overestimated Type 1 and underestimated Type 3 by relying too much on the appearance and too little on the consistency of the lesion. Greater familiarity with the types of lesions will eliminate differences in interpretation.

In our white series there were 34 cases of toxemia. In these cases, infarcts of Type 1 were twice as frequent and infarcts of Type 4 were almost eight times as frequent. Types 2 and 3 showed only a slight increase. This agrees with Hartmann and Siddall's findings in toxemic cases, and lends support to the theory that the more rapid necrosis and autolysis of placental infarcts are responsible for eclamptic toxemia.

In the early part of our study, we were not sufficiently familiar with the early stage of the Type 4 lesion, and consequently classified some eclamptic placentas as negative because of the absence of yellow or gray soft necrotic lesions which represent the later stages of the Type 4 lesion, and are more characteristic of a subacute toxemia. Since learning to recognize the dark purple, spongy, or brown, slightly firmer lesion of acute toxemia, a definite pathologic basis, both in gross and microscopic examination of the placenta, has been found in all cases of pre-eclampsia, eclampsia, and abruptio placentae.

EXPERIMENTAL BASIS FOR THEORY OF PLACENTAL AUTOLYSIS

If eclamptic toxemia is due to poisonous split-products of placental protein, it should be possible to produce the clinical and pathologic

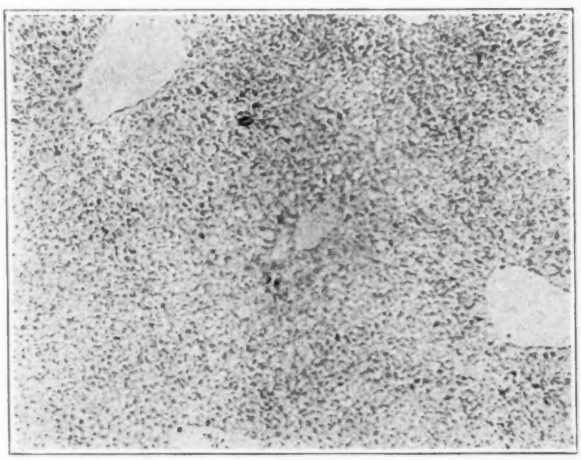


Fig. 17.—Photomicrograph of liver of guinea pig, showing congestion, areas of hemorrhage in mid and outer zone of lobule, fatty degeneration, cloudy swelling and necrosis. Convulsions and death from injections of autolyzed placenta.

manifestations of the disease by the injections of artificially autolyzed placental tissue into susceptible animals.

* * * *

AUTHORS' EXPERIMENTS

In our first experiment, fresh normal placenta was washed free of blood, ground thoroughly, covered with toluene and allowed to autolyze in the incubator at 37° C., for four hours. The toluene was then removed and sterile physiologic-saline solution was added in the proportion of 1-5, and 0.5 per cent tricresol added as a preservative. The preparation was allowed to undergo extraction in the refrigerator for ninety-six hours. The solution was then passed through a Berkefeld filter to insure sterility and the removal of any solid particles before injection.

A rabbit was given intravenous injections of 1 c.c. daily until 10 c.c. had been given. The animal showed no unusual symptoms during the period of the injections or for a period of twenty days thereafter. At the end of this time necropsy was done. The epithelium of the tubules showed marked cloudy swelling, disinte-

gration and desquamation. Hemorrhage was present both between and into the tubules and the glomeruli showed marked congestion and slight hyalinization. The liver showed marked congestion of the bile capillaries and hemorrhages toward the center of the lobules as well as in the periphery. The liver cells showed marked cloudy swelling.

In a second experiment, guinea pigs were used and normal placenta was prepared in the same manner, except that one portion was allowed to autolyze under toluene in the incubator for four hours and another portion for ninety-six hours.

A guinea pig was given four intracardiac injections of 0.5 c.c. of the four-hour preparation, at daily intervals, followed by seven subcutaneous injections of 0.5 c.c. daily. Another guinea pig was injected in the same manner with the ninety-six-hour preparation. Three days after the last subcutaneous injection, both guinea pigs

Fig. 18.—Photomicrograph of kidney (same guinea pig) showing cloudy swelling, necrosis, desquamation of epithelium of tubules, congestion and small hemorrhages between and into tubules.

developed intermittent convulsive seizures, continuing for two hours until death occurred.

The liver cells of the animal receiving the four-hour preparation showed cloudy swelling, marked fatty degeneration and necrosis throughout the entire lobule. Small hemorrhages were present between the liver cords, more marked near the central vein than in the periportal region (Fig. 17).

The tubular epithelium of the kidney showed marked cloudy swelling, disintegration and desquamation. Considerable hemorrhage was present between and into the tubules. The glomerular tufts were engorged with blood which showed early hyalinization and the glomerular epithelium showed pyknosis (Fig. 18).

The liver cells of the guinea pig receiving the ninety-six-hour preparation, showed cloudy swelling involving the entire lobule, distention of the bile capillaries and occasional extravasation of blood.

The tubular epithelium of the kidney showed pyknosis, cloudy swelling and complete destruction of some of the tubules. Hemorrhage into many of the tubules was seen. The glomeruli were apparently normal.

Apparently the products of the four-hour are much more toxic than those of the ninety-six-hour autolysis, which bears out Wells' statement that the products from the early stage of cell necrosis have the greatest toxicity. Chemical changes apparently occurred in the ninety-six-hour preparation, which rendered the products somewhat less toxic to the kidneys and liver, but sufficient to cause convulsive seizures. It is also interesting to note that convulsions did not occur until three days after the last injection.

In a third experiment, extracts were made from ground human liver. A guinea pig was given twelve injections of 5 c.c. each, of a twenty-four-hour autolysate, four of which were given intracardially and eight subcutaneously. Three days after the last injection, the guinea pig was found dead. The liver and kidneys showed essentially the same pathologic picture of marked cloudy swelling, necrosis and hemorrhages as seen in the guinea pigs receiving placental autolysate, except that fatty degeneration in the liver was somewhat less marked than that found resulting from the four-hour placental autolysate.

To determine whether a difference in the clinical and pathologic effects of normal areas and infarcted areas in a placenta from eclampsia could be demonstrated, equal quantities of the normal and the brown infarcted areas from the placenta shown in Fig. 10 were ground in sand and diluted with sterile, normal saline in the proportion of 1 to 5. Tricresol (0.5 per cent) was added as a preservative and the suspension allowed to extract in the refrigerator for forty-eight hours, and then passed through a Berkefeld filter to insure sterility. Guinea pigs were given a daily dose of 1 c.c. subcutaneously, until a total of 20 c.c. had been given. There was apparently no effect on the animals except for some loss of weight. Necropsy was done and the liver and kidneys examined. Pathologic changes were noted similar to those found in the guinea pigs having convulsions, although not so extensive. No marked difference was noted in the effects produced by the normal and the infarcted placental tissue. Inasmuch as the entire placenta was subject to autolysis at intervals during a period of eighteen hours when photographed and examined, the results cannot be taken as evidence against an increased toxicity of the infarcted areas. It is believed that the above experiment, if carried out at once after delivery of the placenta, would show a definite increase in toxicity of the acute infarcts.

It is evident, therefore, that the protein split-products of placental autolysis when injected intravenously or subcutaneously into guinea pigs or rabbits produce poisonous effects, which, both clinically and pathologically, are very similar to those of eclampsia. Objection has been raised by Seitz, Williams and others that similar effects can be obtained by the injection of extracts from autolysis of other organs as well as placenta and also that the injection of unautolyzed placental extract is without effect. In our opinion, this does not constitute any objection whatsoever to the theory of the origin of eclampsia from the products of placental autolysis, since we are probably dealing with protein split-products common to all tissues.

BIOCHEMISTRY INVOLVED IN AUTOLYSIS OF PLACENTA

All tissues during the process of necrosis and autolysis, whether in vivo or in vitro, yield protein split-products which are common to all and are highly toxic. The very cellular tissues such as liver, kidney, spleen, pancreas, etc., autolyze more rapidly and completely and yield more poisonous products than muscle or fibrous tissues. The clinical conditions under which we may have extensive autolysis going on in the body at such a rate that the concentration of the poisonous products overtaxes the natural detoxifying mechanism are relatively few, but the clinical and pathologic effects of severe burns, severe crushing injuries, gangrenous intestine, pancreatic necrosis, acute yellow atrophy of the liver, etc., strongly suggest the overwhelming of the body defenses by highly poisonous protein split-products.

As to the nature of these poisonous split-products, we may gain some information from analyses of placental tissue which have been made by Koelker and Slemons and by Harding and Fort. The latter investigators found the nitrogen content 14.7 per cent, water 9.5 per cent, ash 5.07 per cent, and fat 1.15 per cent. The nitrogen distribution was as follows: amid 6.34 per cent, humin 3.20 per cent, arginine 24.08 per cent, histidine 2.32 per cent, lysine 7.34 per cent, and cystine 1.47 per cent. Total diamino 35.20 per cent, monamino 51.5 per cent, and nonamino 3.47 per cent. Total recovered 99.89 per cent.

They call attention to the strikingly high content of arginine in the placenta, which is about twice that of other organs, and consider that it may be related to the special function of the placenta as an organ of nutrition to the fetus.

According to Wells, all tissues possess the power of self-digestion or autolysis, by virtue of proteases present in every cell. There are two intracellular proteases—one resembling pepsin, which carries digestion to the peptone stage and requires an acid medium of optimum P_H 4.5 to 3.5; the other resembling ereptase, splitting peptones and peptids into amino acids, with optimum P_H 7.8 and not inhibited by acid reaction above P_H 3.*

* * * *

Histamine is produced by the decarboxylation of the amino acid histidine. It occurs in extracts of all tissues, occasionally free, but usually liberated by protein cleavage by acids, ferments or bacteria, particularly of the colon group. It may be extracted with water, saline or dilute alcohol and retains its potency for long periods at ice box temperatures.

* * * *

A striking similarity to many of the effects of histamine, is seen in the acute, severe cases of abruptio placentae complicated by toxemia. The circulatory manifestations are seen in the frequent occurrence of shock, low blood pressure, nausea, vomiting, occasionally of dark bloody vomitus, spasm of the uterus, edema, and hemorrhages on the surface and between the muscle fibers of the uterus and at the placental attach-

*The blood is P_H 7.4 to 7.8.

ment. A moderate amount of blood tinged fluid is often found in the peritoneal cavity.

* * * *

Peptones render the blood noncoagulable when injected into the circulation. This is most significant inasmuch as certain cases of abruptio placentae may show a delayed coagulation time. Mrs. N. developed an acute toxemia during the eighth month of pregnancy. Abruptio placentae developed, and on admission to the hospital the blood pressure was 195-115. Death occurred from toxemia and persistent hemorrhage several hours after a spontaneous labor and delivery, transfusion and other treatment being of no avail. The coagulation time could not be obtained, a specimen of blood standing seventeen hours without showing any evidence of clotting. Needle punctures from hypodermics bled persistently and there was vomiting of dark bloody material during labor. The blood calcium was found to be 7 mg., considerably less than the normal value. There were no platelets. A soft, brown yellow infarct showed the characteristic picture of acute necrosis, disintegration and absence of intervillous substance.

* * * *

CORRELATION OF BIOCHEMICAL AND HISTOLOGIC CHANGES IN ACUTE AND SUBACUTE INFARCTS WITH THE CLINICAL FEATURES OF ECLAMPTIC TOXEMIA AND ABRUPTIO PLACENTAE

Wells studied the relation of autolysis to the histologic changes. There is first a decomposition of the nucleoproteins of the nuclei which is probably brought about by intracellular autolytic enzymes. This is evidently responsible for the deeper staining reaction of the nuclei, the liberated nucleic acid having a greater affinity for the basic stain, and giving the appearance termed pyknosis. Later, the nucleic acids are further decomposed through special enzymes, the nucleases, which probably accounts for the gradual loss in staining power.

* * * *

Considering the variety of protein cleavage products, with various effects such as inhibition of coagulation, vasodilation, vasoconstriction, agglutination of red cells, toxic effect on vessel walls permitting escape of corpuscles and plasma, spasm of the uterus, etc., it is more readily understood why we may have eclampsia without definite convulsions, eclampsia without much if any elevation of blood pressure, shock, variations in degree of albuminuria or edema, the unexpected occurrence of abruptio placentae in the course of what is considered preeclamptic toxemia or the occurrence of eclampsia in the course of what appears to be abruptio placentae, or even nephritic toxemia. It is also probable that histamine or products closely related to it not only account for abruptio placentae but also for the occasional development of edema of

the lungs and petechial hemorrhages in the brain of the eclamptic patient.

It is also clear why the main pathology of eclampsia is seen in the liver, the chief detoxifying organ of the body, and that the pathology in the kidneys supports the view, as stated by Bell, that a soluble toxic substance in the blood is responsible for eclampsia.

* * * *

If the above theory as to the cause and effect of placental infarction and autolysis is proven to be correct, through further clinical, pathologic, experimental and biochemical investigation, it holds out no hope for the control of infarct formation, but emphasizes the imperative need for close observation of patients who develop definite evidence of toxemia, and the necessity of prompt interruption of pregnancy if the toxemia increases. A more specific and effective treatment will be developed only through biochemical research in the recognition and neutralization of the poisonous products of placental autolysis.

CONCLUSIONS

1. Placental infarcts are probably due either to gradual interruption in the circulation of a fetal vessel from the physiologic endarteritis characteristic of the latter months of pregnancy, or to an abrupt interference as a result of rupture, thrombosis or embolism of a fetal vessel, brought about by the trauma of fetal movements on the unprotected fetal vessels on the surface or in the substance of the placenta. Disturbances in the maternal circulation are probably secondary and not primary.

2. Infarction is followed by necrosis and autolysis of the affected placental tissue, thereby liberating poisonous protein split-products such as peptone, histamine, tyramine, guanidine, etc., by virtue of the proteases present in all cells.

3. The physiologic and pathologic effects of these substances are strikingly similar to the clinical and pathologic findings in eclampsia.

4. Slow necrosis, due to physiologic endarteritis, permits thrombosis and the formation of a protective zone of hyaline intervillous substance about the affected villi, thus preventing the diffusion of poisonous protein split-products into the maternal circulation. The villous vessels show very little if any dilatation or engorgement. Such infarcts are firm and white and are not responsible for toxemia.

5. Acute necrosis is probably due to rupture, thrombosis or embolism in a fetal vessel, from trauma of fetal movements. The affected areas first appear dark and spongy, but soon become slightly firmer and of a brown color. Microscopically, the villi show necrosis with congested, dilated or ruptured capillaries and thrombosed vessels. The striking absence of intervillous hyaline substance is probably due to the liberation

of peptone, which has an anticoagulant effect and thereby permits the diffusion of poisonous protein split-products into the maternal circulation, resulting in eclampsia.

6. Toxemia of gradual development, over a period of several weeks, eventually resulting in eclampsia probably differs only in a more gradual necrosis with more evidence of hyaline intervillus substance, and less marked dilatation of villous capillaries and veins. The circulation is probably not completely obstructed. The infarcts in this type are yellow to gray, somewhat soft and are more definitely demarcated.

7. Eclampsia and abruptio placentae probably differ only in the location of the infarcts. In eclampsia, the infarcts are in the substance of the placenta. The intervening healthy placental tissue serves to diffuse the poisonous products, and prevents sufficient concentration of histamine to rupture the decidual sinuses and separate the placenta. Hence, pregnancy continues until eclampsia occurs. If the infarct is in contact with the decidual sinuses, histamine probably brings about abruptio placentae before eclampsia can occur.

8. Injections of Berkefeld filtrate of artificially autolyzed normal placenta into guinea pigs produces stupor, convulsions and death. The pathologic changes in the kidneys and liver are similar to those found in eclampsia. The fact that the injection of autolysates of other organs may produce similar effects in the liver and kidneys of an animal, does not disprove the placental theory of eclampsia, but indicates that the pathologic effects are due to protein split-products common to all tissues, varying somewhat according to the chemical composition of the tissue.

9. It is probable that with a better understanding and recognition of the acute and subacute types of placental infarcts, the association of the same, with preeclampsia, eclampsia and abruptio placentae will be found to be quite constant.

10. If autolysis of placental infarcts is the cause of eclamptic toxemia, it follows that until the specific protein split-products can be successfully recognized and neutralized, emphasis must continue to be placed on prompt interruption of pregnancy before convulsions are threatened.

(For discussion, see page 937.)

The authors wish to express their appreciation to Dr. Lee Bivings, Miss Elizabeth Gambrell, and Miss A. M. Bading for valuable aid in photography, tissue and experimental work; also to those physicians and hospitals whose courtesy and cooperation were of great assistance.

RESEARCHES ON THE TOXEMIAS OF LATER PREGNANCY*

VICTOR JOHN HARDING, D.Sc., F.R.S.C., AND H. B. VAN WYCK, B.A., M.B.,
TORONTO, CANADA

(From the Departments of Pathological Chemistry and Obstetrics and Gynecology, University of Toronto)

THE DIETETIC FACTOR

ECLAMPSIA is a controllable, or partially controllable disease. We are not referring to the decrease in eclampsia noted in prenatal clinics, where the expectant mother is watched monthly or even weekly for any signs of the onset, and where treatment is promptly instituted should any signs be forthcoming. We refer to that great scale experiment in the world war, where the incidence of eclampsia fell from 14 in 1000 to 9 in 1000, in all the big centers of the Central Empires. Even in the postwar period the incidence rose only to its prenatal level, when owing to the greater number of primiparous births it should have been higher. To what cause is this diminution due? The majority of the German and Austrian[1] observers attribute it to the lessened intake of protein and fat. Sweden[2] showed a similar decrease, though Russia,[3] where extreme famine conditions prevailed during the same years, showed an increase.

It has always been a moot question with us that either of these two dietary constituents plays a part in the production of a toxemia of pregnancy. We have not come across one single controlled observation showing that the inclusion of protein or fat in a diet in pregnancy brings on, either an eclamptic seizure, or preeclamptic signs. Those who state that the withdrawal of protein or fat has caused a diminution in preeclamptic symptoms must show strictly the absence of other changes, not only in the diet, but in environmental factors, likely to act favorably. It is not sufficient to conclude that because a carbohydrate diet or a milk diet, given in hospital or even in home treatment, produces good results, that those results are due to a withdrawal of protein or fat. Indeed in proportion to its calories milk contains a large amount of both. Probably the close associations of eclampsia with nephritis, and the older ideas that protein was harmful in the latter disease, resulted in the adoption of a similar view in the toxemias of pregnancy. One notes however, in many centers, that moderate amounts of protein are now allowed. In view of these doubts we proceeded to carry out a series of observations in pregnancy. We proceeded cautiously. We gave normal pregnant women diets high in protein, fat or carbohydrate, but salt-poor (See Tables I and II). The women were under daily supervision in the metabolism ward, and during the period of

*Read, by invitation, at a meeting of the New York Obstetrical Society, February 9, 1932.

dieting were kept in bed. Our results were entirely negative. Neither protein, nor fat produced any symptom of any kind. Carbohydrate was not expected to cause disturbance. In this series of observations it acted merely as a control diet. Our observations and conclusions were not unexpected. Burger,[4] a little time previously, had fed normal pregnant women diets containing 200 gm. of protein without observing any ill-effects, and there must be many women who during gestation take protein in amounts similar to our diets, and remain entirely normal. Clinically it is also of interest to note that not one of our patients suffered from nausea or

TABLE I. DIETS USED IN NORMAL AND TOXEMIC PREGNANCIES

	HIGH PROTEIN	HIGH CARB.	HIGH FAT	
			1	2
Protein, gm.	118	30	46	42
Fat, gm.	38	34	138	104
Carbohydrate, gm.	185	304	57	38
Calory Value	1595	1687	1667	1235

TABLE II. DETAILS OF HIGH PROTEIN DIET

BREAKFAST		DINNER		SUPPER	
	gm.		gm.		gm.
Oatmeal Porridge	60	Scraped Beef	140	Scraped Beef	90
Sugar	10	Potato (boiled)	70	Baked Beans	110
Milk	50 c.c.	Bread	70	Bread	60
Boiled fresh cod	85	Butter	8	Butter	7
Toast	70	Gelatin (diabetic)	1 pkg.	Baked Apple	60
Butter	8	Milk	230 c.c.	Sugar	5
Milk	211 c.c.			Milk	230 c.c.

vomiting when on the high fat diets though some were showing a high degree of "acetone" production. Ketosis will not produce nausea and vomiting of pregnancy.

Our next step was to feed the same diets to patients with mild toxemia.[5] Clinically our patients might have been classified in many ways, hypertension, low kidney reserve, nephrosis, nephritic toxemia, preeclampsia, etc. They were cases however, which would have been subjected to purgation, then given water and afterwards a milk diet, under the ordinary routine of hospital treatment. No purgation was employed. The bowels were emptied daily by simple enemas, which was supplemented by a mild cathartic if necessary. At that time it was our opinion that the semistarvation of such a routine was injurious to the general well-being of the patient. Calories if not supplied in the food, inevitably come from the patient. At no time however did we overstep the patient's calory requirements. The diets contained the minimum amount of salt. Clinically the results were satisfactory. Edemas, hypertensions, albuminurias, all subsided. We should like to point out that at no time have we recommended these diets as specifically curative, or insisted on their

use. Our object was purely demonstrative. The choice of diet can be left to the obstetrician or internist in charge. We merely point out that the choice at his disposal is wide, and fail to see why the patient need live so extensively on her own tissues. Bland and Bernstein[6] also have advocated salt-free diets. They attempted to minimize the factor of hospitalization in their results by keeping the patients in bed on ordinary diet, and allowing them out of bed on the salt-free diet. It was in this latter period that improvement took place. Plass[7] recently has also convinced himself of the innocuousness of protein in the causation of the toxemias of later pregnancy.

What happens when a liberal amount of salt is included?

Everyone is aware of the connection between salt and edema. The work of Ambard, Weil, etc., is well known. All clinical workers know the value of salt-poor diets in the treatment of the edema of nephrosis and of cardiac decompensation. It is known too that the offending part of the salt is the sodium and not the chlorine ion. Other chlorides have no action in producing edema. Other sodium salts, such as bicarbonates and salicylates have this action. The French group of clinicians however had also claimed that a high salt diet was responsible in part for hypertension, and in this country Allen[8] vigorously championed the idea, though later he was compelled to acknowledge the ineffectiveness of salt-free diets in all types.

The normal pregnant woman behaves to a sudden intake of sodium chloride in a perfectly definite manner.[9]

In Table III is shown the approximate water and chloride balance during the seventh, eighth, and ninth day of one of our high protein and carbohydrate diets, on 2 normal pregnant women. It will be seen that the chloride output is approximately 3 gm., and there is an approximate water balance. On the tenth, eleventh, and twelfth day, without any other change in the diet 15 gm. of sodium chloride was added. At once there is a large positive water and salt balance. The body continues to gain water and salt on the next day, though not so greatly, and by the third day of the high salt intake, the equilibrium is nearly complete. What has happened to the water and salt retained by the patient? Blood analysis shows that the blood has become hydrated. The serum proteins have fallen, and the chlorides have risen. Some salt solution evidently has been retained, and the plasma has become diluted. Clinically the patient shows thirst on the first and second days of the high salt intake, but when equilibrium is established the thirst disappears. Occasionally we have caught a fleeting impression of edema in the legs on the first or second day of the high salt intake. Thus the normal pregnant woman adjusts herself to a high salt intake. The nonpregnant individual behaves in a similar manner.

It is the failure of this adjusting mechanism which marks off the toxemias from the normal.

TABLE III. SHOWING APPROXIMATE WATER AND SALT BALANCES ON LOW AND HIGH SALT DIETS IN NORMAL PREGNANCY

WATER INTAKE c.c.	URINE OUTPUT c.c.	APPROX. NACL INTAKE gm.	CL OUTPUT AS NACL gm.		BLOOD ANALYSIS	
					NACL	SERUM PROTEIN
Carbohydrate Diet						
1202	1508	3	3.77	Last 3		
1302	1228	3	3.68	days of	mg. per	per cent
1300	1225	3	3.33	salt-poor	100 c.c.	
3804	4163	9	10.78	diet	479	5.97
	Balance −359		Balance −1.78			
1240	840	+15	7.64	First 3		
1140	946	+15	11.35	days of		
1280	902	+15	10.95	salt-rich		
3560	2688	+45	29.94	diet	489	4.76
	Balance +872		Balance +15.06			
Protein Diet						
1230	972	3	3.88	Last 3		
1230	1360	3	4.21	days of		
1130	771	3	3.54	salt-poor		
3590	3103	9	11.63	diet	472	6.21
	Balance +487		Balance −2.63			
1670	820	+15	7.45	First 3		
1430	990	+15	12.84	days of		
1510	1018	+15	15.34	salt-rich		
4610	2828	+45	35.63	diet	508	5.53
	Balance +1782		Balance +9.37			

CASE 1.—Aged forty-two, para vii, nine months, headache, edema, albuminuria, blood pressure 150/108. Previous pregnancies marked by similar symptoms. Five living children.

The case might be classified as a recurrent toxemia or a low reserve kidney. On milk and orange juice, or on a carbohydrate salt-poor diet the clinical symptoms

rapidly ameliorated. Nine days after admission 15 gm. of salt were added to the carbohydrate diet. Within four days all *the original symptoms returned together with blurring of vision.* Two days after discontinuance of the high salt intake the patient went into labor.

CASE 2.—Aged thirty-two, para v, eight months, edema, and blurring of vision. No albuminuria or rise in blood pressure. Disappearance of symptoms on high protein diet with 3 gm. salt. *Return of edema and general dull heavy feeling on ordinary hospital diet.* Normal labor. Baby weighed 4 pounds 4 ounces. Pregnancies 1 and 3 had been marked by preeclamptic symptoms followed by convulsions.

CASE 3.—Aged twenty-two, para i. Had been on high protein and high fat diets as a normal pregnancy. *Developed marked edema on ordinary hospital diet* on 2 occasions. No other symptoms. Salt-poor protein or fat diet caused disappearance of edema. Normal labor. Baby weighed 4 pounds 8 ounces.

CASE 4.—Aged twenty-four, para ii, seven and one-half months. Admitted with headache, blurring of vision, edema, albuminuria, blood pressure 210/140. Placed on mixed diet salt-poor for nineteen days. Edema almost entirely disappeared. Blood pressure 120/70. Given 30 grams sodium bicarbonate daily with same diet. *Edema returned in three days and blood pressure rose to 176/80 in seven days.* Edema and blood pressure subsided in a week on discontinuance of sodium bicarbonate. A 6 pound macerated fetus delivered 13 days later.

In view of our observations we felt justified in concluding that neither protein nor fat was the causative dietetic agent of toxemia of pregnancy. The action of the sodium salts in causing disturbances however had to be preceded, or accompanied by, some change in the pregnant organism. The normal pregnant woman could resist and set herself at equilibrium at varying levels of salt intake. Whether there is any level at which in the normal, the resistance breaks down and she becomes a toxemic, and whether that possible level is lower than in the nonpregnant condition, we do not know. An intake of 15 gm. of sodium chloride is a high intake. To accomplish this we had to administer part in gelatin capsules. Baird and Haldane[10] observed visible edema in normal man after 35 to 40 gm. salt intake in one day.

We next made observations on the use of hypertonic saline solutions. In other conditions they have been used to relieve intracranial pressure. Would they be of use in eclampsia? According to our previous observations—No! No conclusion in medicine is valid however for all cases and under all conditions. The variation in biologic factors is too great. The arguments pro and con have been set forth in a previous paper.[11] We accordingly gave 300 c.c. of 10 per cent sodium chloride solution to 4 subjects, giving the solution very slowly between the hour of 9 and 11 A.M. A little cracked ice was allowed to allay thirst.

CASE 1.—Normal. Hypertonic saline showed no alteration in any characteristic pointing to a toxemia. A second injection on the following day produced diarrhea but no other signs of disturbance (Chart I).

CASE 2.—Doubtful toxemia. Admitted with slight rise in blood pressure which fell at once on rest in bed with salt-poor diet. The hypertonic saline produced gastric disturbance and headache on the day of the administration. The blood pressure fell to a slightly lower level (Chart I).

CASE 3.—Mild toxemia. This patient had been followed carefully in special clinic, as previous pregnancy had shown toxemia with loss of fetus. Weight changes during pregnancy were irregular. Albuminuria developed and slightly increased blood pressure. Saline was given intravenously morning after admission. Blood pressure, both systolic and diastolic and albuminuria, increased next morning. Epigastric pain, with nausea and vomiting for remainder of day. Headaches for two days. Labor in three days. Living baby (Chart II).

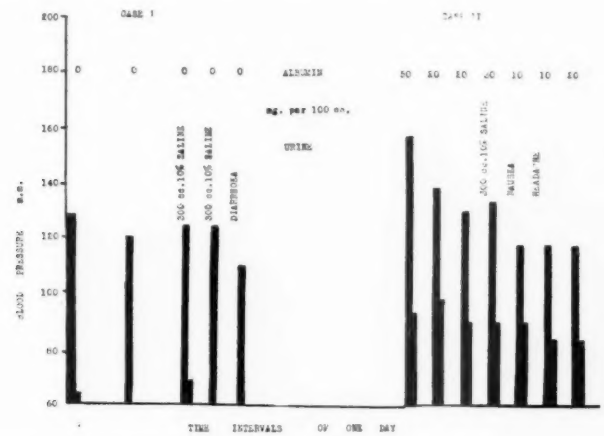


Chart I.—Showing effect of hypertonic saline in normal pregnancy and doubtful toxemia. Columns show systolic and diastolic blood pressure.

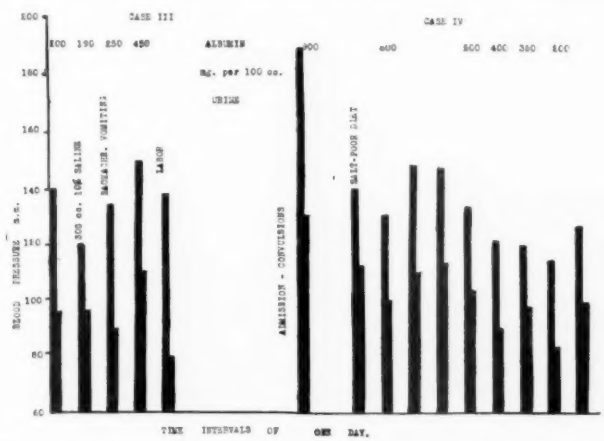


Chart II.—Showing systolic and diastolic blood pressures, etc., in toxemias.

CASE 4.—Eclampsia. Primipara, nine months. Record of 1 convulsion before admission. High blood pressure and albuminuria. No edema. No evidence of liver disturbance. Morphine and gastric lavage on admission. No further convulsions. Placed on mixed ordinary salt-poor diet. Observed for seven days, during which time blood pressure and albuminuria decreased (Chart II). On the eighth day, 18 gm. of NaCl in 300 c.c. of water were given intravenously. Systolic and diastolic blood pressure raised in evening and also next morning. On the ninth day, 30 gm. of NaCl in 300 c.c. of water were given intravenously. Headache, epigastric pain, vomiting almost immediately. Rapid rise in blood pressure throughout the day.

Oliguria. Convulsions at 9:30 P.M. Labor. Baby born at 10:30 P.M. Large amount of fluid from bowel during labor. The nonprotein nitrogen rose from 43 to 60 mg. and the CO_2 combining power dropped from 38 to 29 vols. per cent.[12] Increased albuminuria in next morning's urine. Uneventful puerperium (Chart III).

Again the administration of salt has given no sign of toxemia in the normal pregnant woman, but has intensified or revived the symptoms in the already toxemic. The results in the last case were so dramatic and followed so swiftly on the heels of the injection that we feel we dare not continue our observations in this direction. *The dietetic factor in the production of a toxemia of later pregnancy is neither protein nor fat, but salt.* This is not a new view. Lafont[13] expressed the same view years ago as a result of clinical observation on the difference in the incidence of eclampsia in the European and native population of Algiers.

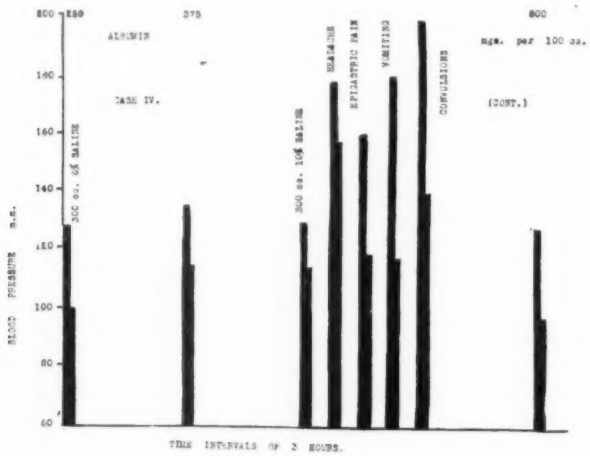


Chart III.—Showing action of hypertonic saline on recovering eclampsia. Columns show systolic and diastolic blood pressure.

All of these 4 women showed a common symptom after the hypertonic saline, a disturbance of the gastrointestinal tract. In the strictly normal pregnancy this took the form of diarrhea, but in the other three, epigastric pain and vomiting. In Case 4 there was a violent outpouring of fluid from the bowel during labor. No analyses of the fluids were made, but it does not seem unreasonable to suppose that the body made an effort to get rid of the excess of sodium by the gastrointestinal route. The gastrointestinal fluids contain considerable quantities of base, consisting chiefly of sodium.[14] Such observations permit us to speculate on the origin of many of those attacks of "acute indigestion" in pregnancy which may usher in eclampsia itself. Do they represent the violent effort to get rid of an excess of base by the gastrointestinal tract, and if so what forces are at work which have brought about the necessity in an apparently normal pregnant woman? The nausea and vomiting of late pregnancy may have its origin in some similar salt and water disturbance.

It is impossible in our present state of knowledge to separate the relationship of sodium salts and water. If sodium salts are retained so is water, even to the point of edema. Are all the symptoms of toxemias of late pregnancy to be explained on a theory of water and sodium retention, a retention resisted successfully by the normal but not by the abnormal pregnancy, and whose abnormality we recognize under the general heading of toxemia? Such a view is akin to the old view of Traube and Rosenstein[15] revived in a more modern form by Zangemeister.[16] Does a study of some of the suggested forms of therapy reveal any such indication?

TREATMENT

In discussing the different forms of treatment we have no intention of contributing to that perennial discussion, radical or conservative measures. Our discussion is limited to types of therapy which seem to have a relationship to the possible action of sodium salts or changes in the water balance.

A. SPECIAL THERAPEUTIC MEASURES

(a) *Venesection.*—This old method of treatment is now in little use. Those who offer any defense at the present day consider it only of use if a large amount of blood is removed. It would be under the condition of a large venesection that the procedure would be of most value in removing both sodium salts and water. The variation of Irving and Taylor,[17] in which the corpuscles are replaced in the patient might perhaps be improved by using isotonic glucose solution instead of normal saline.

(b) *Purgation.*—Under ordinary conditions the loss of water and sodium salts by the bowel is very small. Under conditions of diarrhea the loss may be considerable. Magnesium sulphate is to be preferred, at present, though we should like to see observations on the use of potassium acid phosphate.

(c) *Sweating.*—The use of hot packs, etc., has been almost entirely discontinued. Yet profuse sweating will remove moderate amounts of water and sodium salts. The procedure of hot packs however, is troublesome and is somewhat disturbing to the patient, whereas importance of administering treatment without disturbance is a recognized essential. The results obtained are usually not commensurate with the effort, yet we believe modern hydro- or electro-therapy might develop conditions, which would be of service in some cases.

(d) *Intravenous Magnesium Sulphate.*—Lazard and others[18] have reported enthusiastically on the use of this compound. There are evidently limitations to its use however.[19] In our opinion its success is due to the diuretic effect of the SO_4 ion, and the sedative action of the Mg. ion.

(e) *Intravenous Glucose.*—Titus[20] for some time has advocated the use of hypertonic glucose solutions given intravenously. His original reason was to maintain the liver at as high a glycogen content as possible. More recently he has claimed a relative hypoglycemia as an actual cause for the convulsions. Quite apart from the controversy on his assumptions and biochemical findings, the giving of glucose in large and sudden quantities produces changes other than in the carbohydrate metabolism. It is these changes which may be helpful. One of us in experimenting with doses of glucose at different times of the day has noticed the production of an anuria followed by a profuse diuresis following its use. The period of anuria was accompanied

by a marked dryness of the skin. We interpret this as a shift of water from the peripheral vessels to the central areas, which water afterwards becomes available for the production of urine. The anuria which can be produced in this way has been previously noted in rabbits.[21] The use of insulin combined with glucose to combat the acidosis of eclampsia was advocated by Stander and Duncan, etc.[22] The addition of insulin to the glucose may ensure the same changes with small amounts of glucose, which Titus obtains with the more concentrated solutions.

(f) *Ammonium Chloride.*—This was recommended by Mussey[23] in a dose of 10 gm. a day. It has a well-known diuretic effect on account of its acid producing properties. It will reduce edema, but Mussey is of the opinion that the changes brought about by the ammonium chloride extend beyond the simple reduction of edema. Other ammonium salts might be of use. The chloride is difficult to administer on account of its unpalatability. Harding and Silverthorne[24] showed that ammonium acid phosphate in large doses produced lowering of the CO_2 combining power of dogs similar to that produced by ammonium chloride. Scott[25] recommends the phosphate for the production of acid urines in the treatment of pyelitis, stating the unpalatability of this salt is much more easily disguised. As in the use of ammonium chloride, observations on the CO_2 combining power would be necessary to make sure that too large a dose of phosphate is not given. We feel however, any rise in the blood urea need not produce alarm. Indeed a raised blood urea may be helpful in maintaining diuresis.

B. NUTRITIONAL THERAPEUTIC MEASURES

(a) *Milk.*—The use of milk inevitably means the use of a low calorie medium-protein sodium-poor diet. How far beneath the calorie requirements of the woman the milk diet may fall, depends upon more than one factor. A liter of milk contains 35 gm. protein, 50 gm. carbohydrate, and 35 gm. fat. Its calorie value is 655. Two liters of milk a day would be the maximal amount which any average sized woman could take. Indeed from 1200 to 1500 c.c. would be a considerable intake, a calorie value of 900 to 1300. This would be considerably under the calorie requirements of all but the very smallest of women. Only our fat diet No. 2 approximates this in calorie value. The calorie requirements of a woman during pregnancy are variable. In general they increase per kg. of body weight as pregnancy progresses. As a general calculation the nonpregnant woman in bed would require 28 calories per kg. per day as a basal diet. It would be underestimating the resting calorie requirements of the pregnant woman at 30 calories per kg. per day. A 60 kg. (132 pound) woman would thus require 1800 calories. Thus practically all women are undernourished on a milk diet.

(b) *Starvation.*—This is part of the treatment as advocated by the Dublin School.

(c) *Starvation and Water Deprivation.*—This, carried out over a period of three days, has recently been advocated by Seitz[26] and by Baumgart[27] for severe toxemias. It is in conformity with some of the methods of treatment of nephritis. It is im-

TABLE IV. GERMAN WAR DIET

	GRAMS	PROTEIN	CALORIES
Bread	271	17.2	688
Potatoes	357	7.5	341
Butter and Margarine	11.4	——	89
Meat	36	4.5	78
Eggs	——	1.0	13
Sugar	26	——	104
Cereals	9.8	0.9	31
Totals		31.1	1344

portant because it represents a conscious effort to rid the body of cellular water as well as edema fluid. The restriction is unquestionably irksome, but in actual eclamptics is probably not so irksome as it sounds, on account of the semicomatose condition during part of the time. The treatment of a potential eclamptic by this method, who feels well and who perhaps is barely persuaded of the gravity of her position, would be difficult.

(d) *The "War Diets" of the Central European Empires.*—The war diets fell far short of the amounts planned by the German and Austrian physiologists. They were low in protein and fat, but how inadequate they were in calories is not so generally known. The rationed diet, as actually supplied is shown in Table IV.[28] In calorie value it is at least as low as the milk diet used in preeclamptic therapy.

(e) *Salt-poor Diets.*—These have already been discussed.

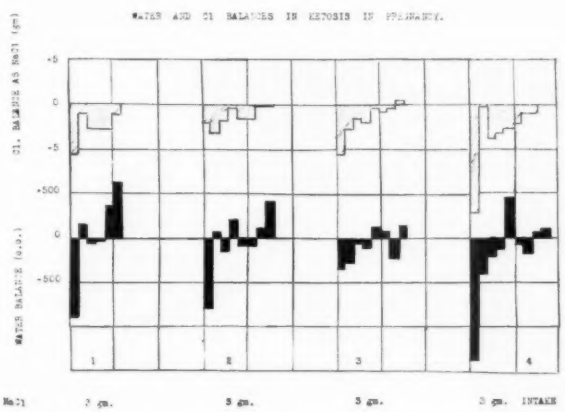


Chart IV.—Showing water and Cl balances in normal pregnancy on salt-poor ketone-producing diets. Previous diet of subjects 1, 2, 3 was salt-poor. Previous diet of Subject 4 was salt ad lib.

In the foregoing résumé of some therapeutic measure we have shown that many either consciously or unconsciously remove water, and thus sodium salts. Common to all the diets we have mentioned is the factor of undernutrition, sometimes moderate, sometimes severe. Is the undernutrition as valuable as the absence of salt? Is eclampsia to be regarded, partially, perhaps as a disease of overnutrition or plethora? If so the ideas with which this work was commenced may require some revision. In presence of severe undernutrition the possibility of another factor enters into our discussion, the production of ketosis and the removal of cellular water. In the starvation treatment of Tweedy, Seitz, Baumgart, etc., ketosis must certainly be present. It is well known, especially since the work of Gamble, Tisdall and Ross[29] that in presence of the ketosis of starvation, water leaves the cells of the body. A change in the water balance is also noticed in diets high in fat. Benedict and Milner[30] showed that losses of body water occurred, when the 67 per cent of the calorie needs were derived from fat. This point is certainly reached in many of the undernutrition diets we have been mentioning. Harding, Allin, Eagles and Van Wyck[31] noticed losses of water on the first

day of a high fat diet in normal pregnancy even if the previous diet had been salt-poor. If the sodium chloride intake is kept low and constant, there is also to be noted a continuous negative chloride balance (Charts IV and V). The balance changes when the low sodium chloride intake is changed to a high intake. These observations would support the idea that a certain degree of ketosis might be beneficial.

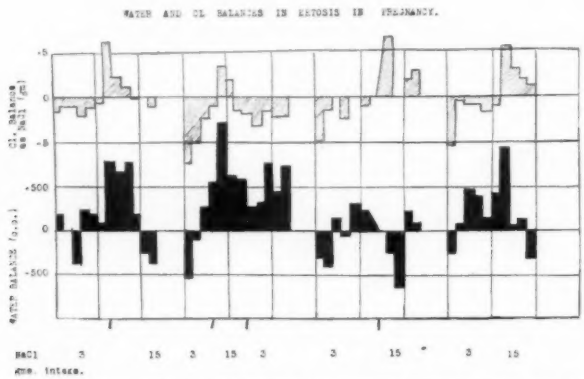


Chart V.—Showing water and Cl balances in normal pregnancy on ketone-producing diets, with alternations in intake of sodium chloride.

It is interesting to notice at this point the analogy which has developed between the partial etiology of epilepsy and eclampsia. Ketone-producing diets are claimed to be beneficial under controlled conditions in the treatment of epilepsy.[32]

We have not made any prolonged observations on the effect of ketone-producing low salt diets on the toxemias of later pregnancy. We have shown that they are harmless in normal pregnancy. One of our diets is of very simple composition, is naturally almost salt-free and is liquid, thus allowing easy control.

	Cream (32%)	320 gm.	Protein	40 gm.
Calories 1546	Whole Milk	670 gm.	Carbohydrate	45 gm.
	Egg White	85 gm.	Fat	129 gm.

Such a mixture can be given in small quantities throughout the day to any desired amount.

A possible criticism will present itself. A ketone-producing diet will often lower the level of the plasma bicarbonate. The plasma bicarbonate in actual eclampsia is sometimes at acidosis level. Obviously care should be maintained under those conditions. Observations in our own laboratory (unpublished) have shown us that large doses of urea will raise temporarily the CO_2 combining power of the plasma. Urea is also a powerful diuretic. It is harmless in a normal pregnancy and in a mild toxemia, according to our few observations. It has been used in the treatment of epilepsy in combination with ketone-producing diets by McQuarrie,[32] Maclean,[33] Crawford and McIntosh[34] and Feilchenfeld[35]

have administered it freely in nephrosis. There is thus no reason against its use. We should recommend a dose of 60 grams urea and 10 grams of citric acid in 10 per cent solution in 10 divided doses per day. The presence of the citric acid makes the urea solution more palatable.

The suggested use of high fat diets would probably be better applicable to thin or moderately nourished women. Heavy, overweight women would probably be benefited more by severer restrictions.

WEIGHT CHANGES IN RELATION TO THE TOXEMIAS

The series of observations in the preceding sections can be interpreted as favoring Zangemeister's theory. In its later form, "hydrops gravidarum," he attempts to explain the symptoms as a form of edema. One important feature of Zangemeister's ideas is the possibility of recognition of a toxemia of later pregnancy by following the weight changes of the patient. Abnormal gains in weight are an index of an oncoming toxemia. Observation of the weight of the patient is well known as a clinical test of impending edema in other diseases. Confirmation of this part of Zangemeister's views has come from many quarters. Moreover water retention evidently plays a part, or at least accompanies, toxemic signs other than edema. De Wesselow and Wyatt note "in some apparently nonedematous cases of eclampsia water may therefore be present in spite of the clinical findings." This observation was made as a result of their study of water balances in the puerperium.

If there is so much evidence in support of Zangemeister's view, why has it not gained more general acceptance? We know many prenatal clinics where no record is kept of the patient's weight. The somewhat casual attendance of ignorant patients at an outdoor clinic certainly militates against the correct collection of data of this kind, but even in many private practices where conditions are favorable, the use of scales and the charting of weights is by no means universal.

Increases in weight during pregnancy are variable, depending on many factors; age, dietetic habits, exercise, presence of infection as well as variations in the general tendency to put on weight during pregnancy. The general gain in weight varies from 3½ to 5 pounds a month. Kerwin's[36] average figure for 127 pregnancies is 2 pounds a month in the latter half of pregnancy. Davis[37] has stated that a gain per month of 7 to 7½ pounds or over is pathologic in character. Bingham[38] has recently stated that gains of over 4 pounds a month are to be considered abnormal. There is evidently a wide variation in opinion on normal standards. Our records of three normal pregnancies and one toxemia are shown in Chart VI. At a glance it is impossible to distinguish the normal from the toxemia. Both Subject III and Subject L show monthly gains of over 7 pounds. Nor do the fortnightly records show up any essential difference. Indeed of the two it is the normal pregnancy which shows more consistently the large gains. Zangemeister's

views may enable the obstetrician to distinguish the preedematous stage of a grossly water-logged toxemia, but it apparently fails to warn him of a toxemia such as is present in Subject III, if Subject L is to be considered normal. Yet Subject III was one of the patients whose albuminuria and blood pressure was increased by the hypertonic saline

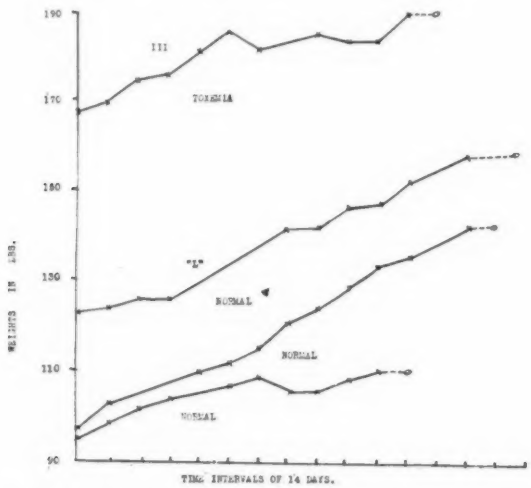


Chart VI.—Showing weight changes during pregnancy.

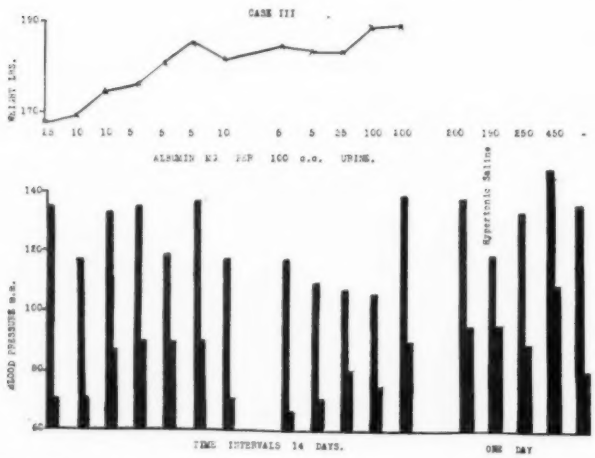


Chart VII.—Showing development of toxemia under ordinary conditions and its exaggeration by hypertonic saline.

treatment. Fundamentally this case should be an example of water retention, but before dismissing Zangemeister's ideas entirely, let us examine the collected data as shown in Chart VII, a little more closely.

The first 5 recorded weights show a period of active gain, with a normal content of albumin in the urine and a fluctuating blood pressure, which just fails on 4 occasions to reach the accepted danger point of

140 mm. Next, the weight is practically stationary with a markedly decreasing blood pressure. There is a normal albuminuria until ten weeks after the highest recorded weight. Then albumin appears in the urine in an amount just over the normal limit. In the next fortnight there has been a gain in weight and now the albumin is marked. A week later the blood pressure has risen to 140 mm. and the albuminuria has further increased. Note that the developing toxemia is now showing itself in the kidney rather than in the blood pressure. It was at this point that the patient was brought into the hospital. Can we interpret the weight changes in accordance with the development of the toxemic symptoms? The period of approximately constant weight was not marked by an infection, a common source of loss of weight of which an example is shown in one of the "normal" curves. The period of constant weight may be interpreted as a balance between the normal weight gains of pregnancy and a loss of fluid accumulated in the fore period. The loss of fluid lowers the extravascular pressure and the blood pressure falls. The toxemia, however, has been initiated and shows itself at the patient's weakest point, the kidneys. Such might be one interpretation. Ten weeks however have elapsed since the end of the period of rapid weight gain. This seems a long time to wait for evidence of the kidney disturbance, especially when other signs point to improvement. It seems more probable to us that in addition to general gains in water, local gains in water can be made by the different organs. These excessive local gains may be made even when the weight chart shows only the normal increases, or in such a subject, as this, no increase at all. If such be the interpretation it renders impossible the early detection of every toxemia by a study of weight charts. Only those cases can be detected of which one of the symptoms is a generalized water retention. Whether a generalized retention of water always precedes or accompanies the localized disturbance, we have no evidence.

Of intense interest to us is the evident connection between the toxemia, as it developed naturally in this patient and its exaggeration as seen in hospital under the influence of the hypertonic saline. We have just pointed out how, after some slight increase in blood pressure, which subsided, the toxemia developed suddenly in the kidney. The disturbance affected the blood pressure to a lesser degree than the kidney. After the hypertonic saline, the blood pressure increased, unmistakably, but the major effect was the increase in the albuminuria. *The action of the hypertonic saline was to exaggerate the toxemia in the direction in which it was proceeding under natural conditions.*

That such small localized changes in water distribution affecting single organs rather than the whole vascular system can occur is rendered more probable when we find that rapid shifts in water can be observed occurring over the whole body. We published in another paper an account of an unusual fluctuation of symptoms in a toxemia occur-

ring in one of our colleague's patients. In the presence of a generalized edema, the blood pressure fell. When in the space of twenty-four to forty-eight hours the edema subsided, the blood pressure rose to the point of convulsions.

Zangemeister's ideas therefore need not be discarded, but we believe they require modification. The excessive gain in weight may affect the whole body, but it may also be localized, perhaps without any such general weight increase. Following the preedematous stage in any one organ, comes hemorrhage and necrosis, such as is recognized at autopsy. The theory requires modification to allow for changes in the *internal* distribution of water, as well as changes brought about by *external* agencies. Such a view allows the possibility of a common origin to the usual toxemic disturbances, and also to anemias of pregnancy, accidental hemorrhage and the development of true diabetes in pregnancy.

We have attempted to interpret the toxemias of pregnancy in terms of a water or sodium balance. We recognize that even if our interpretation is true, it only represents one phase of a complex problem.

CONCLUSIONS

1. Observations on the effect of added salt to the diet, or on the use of hypertonic saline solutions show, that the normal pregnancy remains normal, and that the toxemic pregnancy has an exaggeration of symptoms.

2. A study of many of the older and some of the more recently suggested forms of treatment shows that they cause the removal of water from the body, or may be involved in some change in the internal distribution of water.

3. The "edema" theory of Zangemeister, at present, offers the most unifying view of the toxemias of later pregnancy. It requires modification, however, to allow for the formation of edema in individual organs, apart from a generalized water retention, and for the possibility of internal changes in water distribution.

4. Further progress might be made by a more intensive study of the atypical forms of toxemia and by a wider acceptance both in theory and in practice of the value of observations of weight during pregnancy.

5. The variability of the toxemias of later pregnancy is in harmony with the assumption that they possess one origin and a multiplicity of symptoms.

The authors wish to express their indebtedness to the Medical Research Committee of the University of Toronto for assistance during the progress of these researches.

REFERENCES

(1) *Hinselmann, H.:* Arch. f. Gynäk. **117**: 443, 1923. (2) *Groene, O.:* Svenska Laekartidningen **20**: 769, 1923. (3) *Bublitschenko, L.:* Monatschr. f. Geburtsh. u. Gynäk. **49**: 139, 1925. (4) *Burger, K.:* Zentralbl. f. Gynäk. **47**: 260, 1923. (5) *Harding, V. J., and Van Wyck, H. B.:* J. Obst. & Gynec. Brit. Emp. **33**: 17, 1926. (6) *Bland, P. B., and Bernstein, M.:* Am. J. M. Sc. **173**: 844, 1927. (7) *Plass,*

E. D.: (Private Communication.) (8) *Allen, F. N.:* J. A. M. A. **74**: 1652, 1920. *Allen, F. N., and Sherrill, J. W.:* J. Med. Research **2**: 429, 1922. (9) *Harding, V. J., Allin, K. D., and Van Wyck, H. B.:* J. Biol. Chem. **62**: 61, 1924. (10) *Baird, M. M., and Haldane, J. B. S.:* J. Physiol. **56**: 259, 1922. (11) *Harding, V. J., and Van Wyck, H. B.:* Brit. M. J. **2**: 589, 1930; Canad. M. A. J. **24**: 635, 1931. (12) *c. p. Odaira, T.:* Tokohu, J. Exp. Med. **4**: 523, 1924. *Hanzlik, P. F., De Eds, F., and Tainter, M. L.:* J. Pharmacol. Exper. Therap. **21**: 217, 1923. (13) *Lafont:* Quoted by Kosmak, ref. (3) p. 51. (14) *Gamble, J. L., and McIver, M. A.:* J. Exper. Med. **48**: 837 et seq., 1928. (15) *Traube and Rosenstein:* See Stander, H. J., Toxemias of Pregnancy, 1929, Williams and Wilkins, p. 87. (16) *Zangemeister, W.:* Ztschr. f. Geburtsh. u. Gynäk. **81**: 491, 1919; Deutsche med. Wchnschr. **47**: 549, 1921; Zentralbl. f. Gynäk. **49**: 225, 1925; Lehrbuch. f. Geburtsh. 1927. (17) *Irving, F. C., and Taylor, J. V.:* Am. J. Obst. & Gynec. **17**: 767, 1929. (18) *Lazard, E. M.:* Am. J. Obst. & Gynec. **13**: 720, 1927. *Lazard, E. M., Irwin, J. C., and Vruwink, J.:* Am. J. Obst. & Gynec. **12**: 3, 1926. (19) *Stander, H. J.:* Toxemias of Pregnancy, 1929, Williams and Wilkins, p. 132. (20) *Titus, P., Dodds, P., and Willetts, E. W.:* Am. J. Obst. & Gynec. **14**: 89, 1927; **15**: 303, 1928. *Titus, P., Willetts, E. W., and Lightbody, H. D.:* Am. J. Obst. & Gynec. **19**: 16, 1930. *Titus, P.:* Am. J. Obst. & Gynec. **17**: 553, 1929. (21) *Fisher, G., and Wishart, M. B.:* J. Biol. Chem. **13**: 56, 1912-13. *Mendel, L. B., and Rose, W. C.:* J. Biol. Chem. **10**: 213, 1911-12. (22) *Stander, H. J., and Duncan, E. E.:* Am. J. Obst. & Gynec. **10**: 823, 1925. *Vogt, E.:* Klin. Wchnschr. **6**: 1339, 1927. (23) *Mussey, R. D.:* Am. J. Obst. & Gynec. **11**: 222, 1926. (24) *Harding, V. J., and Silverthorne, L. N.:* J. Pharmacol. & Exper. Therap. **36**: 525, 1929. (25) *Scott, J. W.:* Canad. M. A. J. **24**: 548, 1931. (26) *Seitz, L.:* Arch. f. Gynäk. **142**: 52, 1930. (27) *Baumgart, G.:* Zentralbl. f. Gynäk. **53**: 647, 1929. (28) *Lusk, G.:* Physiol. Rev. **1**: 523, 1921. (29) *Gamble, J. L., Ross, G. S., and Tisdall, F. F.:* J. Biol. Chem. **57**: 633, 1923. (30) *Benedict, F. G., and Milner, R. D.:* U. S. Dept. Agric. Offic. Exp. Stat. Bull. **175**: 224, 1907. (31) *Harding, V. J., Allin, K. D., Eagles, B. A., and Van Wyck, H. B.:* J. Biol. Chem. **63**: 37, 1925. (32) *McQuarrie, I.:* Am. J. Dis. Child. **38**: 451, 1929. (33) *Maclean, H.:* Modern Methods in Diagnosis and Treatment of Renal Diseases, London, 1924, Lea and Febiger. (34) *Crawford, J. H., and MacIntosh, J. F.:* Arch. Int. Med. **36**: 530, 1925. (35) *Feilchenfeld, J.:* Therap. d. Gegenwort. **59**: 273, 1918. (36) *Kerwin, W.:* Am. J. Obst. & Gynec. **11**: 473, 1926. (37) *Davis, C. H.:* Am. J. Obst. & Gynec. **6**: 575, 1923. (38) *Bingham, H. W.:* Am. J. Obst. & Gynec. **23**: 38, 1932.

(For discussion, see page 945.)

Mgalobeli, M.: The Influence of Employment in Tobacco Factories on the Reproductive Organs of Women. Monatschr. f. Geburtsh. u. Gynäk. **88**: 237, 1931.

Tobacco is a poison and affects the gonads. The social surroundings, however, are also important. In the large series of cases studied by the author an equal number of abnormalities was found in those who stood up during their work and those who sat down. Menstrual disturbances were very common. The more the women came into contact with tobacco dust and the worse the home surroundings, the more leucorrheal discharge they had. The number of pregnancies and labors were diminished and there was an increase in the frequency of spontaneous abortions and deaths of children from one to three years of age. All of these conditions are definitely attributable to the direct or indirect effect of nicotine on the sex organs. The author urges that girls up to the age of 18 should not be permitted to work in tobacco factories. Furthermore women employed in such factories should not be permitted to remain in any one position during work for a long time. There should be frequent periods of rest and where possible these should be combined with compulsory gymnastic activities. To avoid direct irritation of the genitalia the author advises that the women workers wear proper undergarments.

J. P. Greenhill.

THE RELATION OF THE ANTERIOR LOBE OF THE HYPOPHYSIS TO GENITAL FUNCTION*

BERNHARD ZONDEK, M.D., BERLIN, GERMANY

I CONSIDER it an honor to be asked to speak on my hormone studies before an American audience, because of the outstanding discoveries which have been made in the United States in this field of research. Without American investigators the modern study of the sexual hormones would have been impossible. May I be permitted to mention but a few of those whose work was of great importance to me, namely Leo Loeb, Robert T. Frank, Evans, P. E. Smith, Stockard and Papanicolau, Long and Evans, Allen and Doisy, Engle, and Corner.

Within the limited time given, I can speak only of those of my researches and their results made within the last few years.

Having succeeded in preparing an aqueous extract of ovarian hormones (folliculin), I found that with it the estrus could be produced in infantile animals but notwithstanding this artificially procured sexual prematurity, the ovaries themselves remained unaffected. The impulse which starts ovarian activity does not originate in the ovary but somewhere else, namely, as I discovered, in the anterior lobe of the hypophysis. I shall not dwell on the details of these studies but desire to state merely my final conclusion, namely, that the anterior hypophyseal lobe is the motor impulse for sexual function. Its hormones represent the superimposed, nonspecific, general, sexual hormones. The hypophyseal hormones are primary, the specific sexual hormones are secondary factors.

Introduction of anterior hypophyseal substance in the infantile rodent results in three morphologic and functional effects: HVR I = ripening of follicle and start of estrus, HVR II = hemorrhages in enlarged follicles ("blood points"), and HVR III = formation of corpora lutea,—luteinization. The practical importance of these effects lies in the fact that these three specific reactions are available as an exact test (Zondek-Aschheim) for the presence of anterior hypophyseal hormones and thus have made it possible to study the relation of the anterior hypophyseal lobe to the organisms. By means of this test I succeeded in developing a chemical isolation of the anterior lobe hormone, to which I gave the name "Prolan." In comparison with folliculin, prolan is a sensitive substance which is destroyed by a temperature over 60° C. It can be produced in sufficient purity to render it available for clinical use. However, I shall not speak of clinical problems, and refer the interested reader to my book,

*Read, by invitation, at the Fifty-Seventh Annual Meeting of the American Gynecological Society, Quebec, Can., May 30 to June 1, 1932.

Die Hormone des Ovariums und des Hypophysen-Vorderlappens. (Berlin, Springer, 1931.)

Of late the chemic identity of the prolan produced by the hypophysis and that extracted from the urine of pregnant women has been questioned, though both yield the typical reactions HVR I to III. While Evans, in hypophysectomized rats, observed an ovarian effect decidedly more marked with anterior lobe extract than with pregnancy urine, Hill and Parkes, in hypophysectomized rabbits, failed to notice any difference. Most interesting is Evans' observation that the hypophyseal growth hormone intensifies prolan reactions; a fact which points to a close interrelation between these hormones. It seems that the definite answer in regard to chemic identity of lobe and urine extracts will not be forthcoming until both these substances will be available in chemically pure form.

Chemical analysis likewise will solve another problem; whether prolan is a single hormone or a mixture of two, as we assume from biologic effects, namely, a hormone "A" causing ripening of follicles, and a hormone "B" causing luteinization. It is possible that we are dealing with different isomeres of the same molecule. Assumption of a duality of prolans explains to us also why the ovary produces hormones, the one of the follicle and the other of the corpus luteum. Thus hormone A (the folliculation hormone) would be the controlling sexual hormone which, through folliculin, leads to the proliferation phase, while the luteinizing hormone B through the contained progestin, starts the functional phase and later exerts a protecting influence over the implanted ovum.

Objections have been raised to our conception (Zondek and Aschheim) of the anterior lobe as the activating motor for sexual function. Some investigators assigned to the maturing ovum supremacy in the generative process, others vested it in the corpus luteum. Without doubt, as I emphasized in my book, the anterior lobe of the hypophysis is influenced also by ovarian hormones, so that folliculin might stimulate or retard the output of anterior lobe hormones. However, in view of the mutual interdependence of all endocrine glands and of the fine gradation of their chemic output, it is not surprising that interrelations between these glands are manifold as well as intimate. As I have expressed it, the motor of sexual function is regulated also by its own products. Nevertheless, the fact remains that the anterior lobe exerts superior authority over the genital sphere. This can be deduced, e. g., from the following experiments: Removal of the hypophysis ends all functional activity of the sex gland. Without a hypophysis, there is no follicle maturation, no impregnation. If, on the other hand, the sex gland is removed, the anterior hypophyseal lobe not only keeps on functioning but, indeed, puts out more prolan. With prolan, as previously shown, we can initiate every phase of the genera-

tive cycle. The follicle is made to mature and to rupture. The liberated ova migrate through the tubes into the uterus (Figs. 1 and 2). In collaboration with Boeters I succeeded even in the fertilization of such ova in an infantile animal and thus a pregnancy was produced in an infantile rat by means of prolan (Fig. 3). With prolan we were able also to induce follicle maturation and liberation of ova even in the pregnant animal and thus to annihilate the generally accepted law of ovarian dormancy during pregnancy. By means of prolan in senile animals the quiescent ovarian activity can be restored with rhythmic return of the estrus. All these

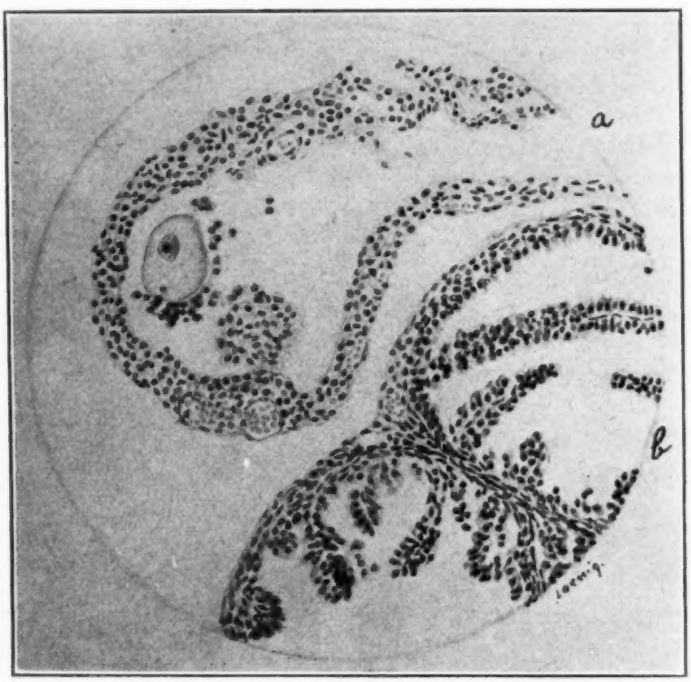


Fig. 1.—Section of tube from an infantile mouse after treatment with prolan (a) fimbria, (b) tube. The artificially liberated ovum in the fimbria.

facts, established in experiments, seem to support our contention of the supremacy of the anterior lobe over the sex gland.

With some certainty we can designate in the anterior lobe the part producing the prolan. It is elaborated by the basophilic cells, as proved in the following experiment: I implanted posterior lobe of the hypophysis of the human being and of cattle into infantile mice. The head part of the posterior lobe fails to cause HVR I to III. On the other hand, that part of the posterior lobe which is immediately adjacent to the anterior lobe contains prolan only in the human being and not in cattle. As demonstrated by Berblinger, in the human being but not in cattle, cell strands run from the anterior into the posterior

lobe, these strands consisting entirely of basophilic cells. This, in my opinion, justifies the deduction that in the human being it is the basophilic cells which produce prolan. Evans and Simpson, also Berblinger, after various experiments also arrived at the conclusion that the basophilic

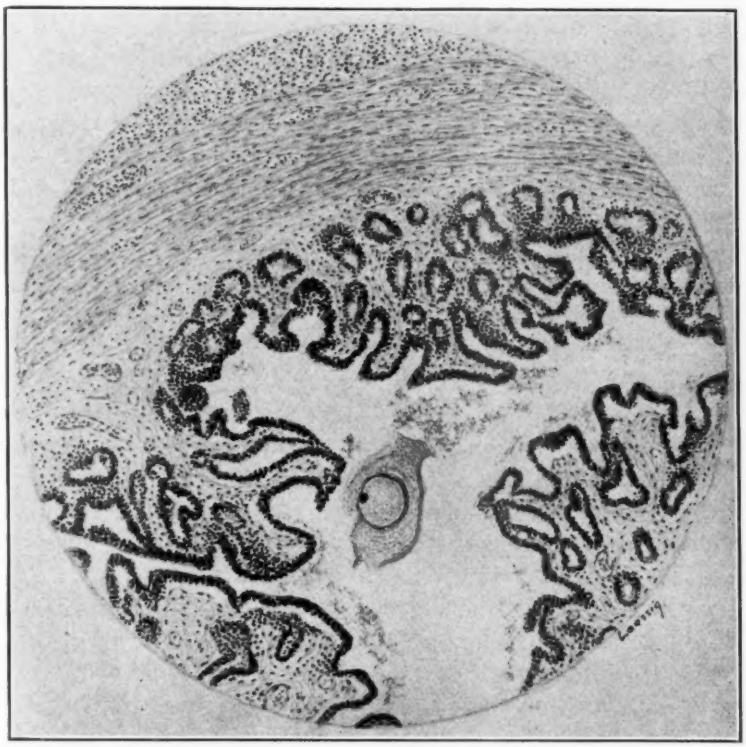


Fig. 2.—Section of infantile rabbit uterus after treatment with prolan. The artificially liberated ovum in the uterine cavity.

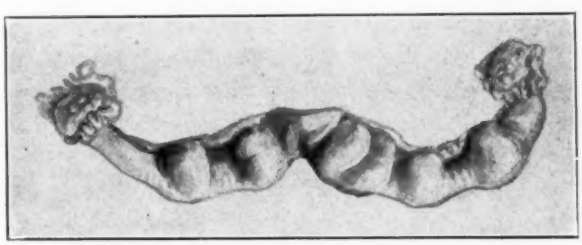


Fig. 3.—Genital organs of infantile rat after treatment with prolan and fertilization. Six embryos in the uterus.

cells in the anterior lobe furnish the prolan, though according to Kraus the eosinophilic cells likewise possess this faculty.

Prolan exerts an effect also on the male sex apparatus. But this effect, as shown likewise by P. E. Smith, Steinach and Kun, Borst, Doederlein and Gostimirovic, is not as characteristic in the male as it is in the female.

We might obtain with prolan some enlargement of the testicles and marked proliferation of the prostate and particularly of the seminal vesicles, even spermatogenesis may seem to be stimulated in infantile animals, but it is impossible to achieve prematurely, full maturation of spermia. With an increase of the dose of prolan, the enlargement of the testicles can be augmented, but this is the result solely of hypertrophy of the interstitial tissue and not of the generative tissues. Both in woman and in man, this prolan effect reaches the sexual organs solely by way of the sexual gland. Prolan exhibits no effect in the castrated buck. From investigations carried out with Boeters we conclude that hormone A influences the generative and hormone B the interstitial apparatus together with the adjunct organs of the testicle.

Reactions HVR II and III form the basis for the hormonal pregnancy test made with urine. Since this method is well known in America, further remarks would be superfluous. It is indeed a method for early diagnosis, because it is found to be positive within five or six days after nonappearance of the expected menstrual flow. Reports from the literature of the world prove that the test is correct in about 98 to 99 per cent, which probably represents the optimum for any biologic method. Two objections to the method have been advanced: (1) some urines are too toxic to be injected, amounting to approximately 6 to 7 per cent of all specimens; (2) the test takes four days. These disadvantages I eliminated by extracting the toxic substances with ether and adding a 3 per cent solution of dextrose. This procedure makes all urines available for the test and also reduces the time for reactions from four to three days. I desire to call attention to a recent improvement in technic. If I am not quite certain whether the ovary of the injected infantile mouse contains a "Blutpunkt," or hemorrhagic spot, I remove it and after washing in water place it in glycerin. In this manner the tissue clears up and the spots, when present, become visible through the contrast in color. In case of doubt, a corpus luteum can be made visible in the excised ovary by squeezing it between two glass slides. The follicles under pressure appear as spherical clear spaces, the corpora lutea as darker and larger formations. In looking on them under the microscope the diaphragm should be almost closed.

A noteworthy modification of the Aschheim-Zondek pregnancy test here in America has been introduced by Friedman and Schneider. They inject the urine not subcutaneously into mice but intravenously into rabbits. The time required for the test is thus reduced to one or two days.

By means of the hormonal test we can diagnose not only the normal but as well the pregnancy which pathologically has changed into hydatiform mole or its sequela, a chorionepithelioma. The hydatid degeneration of chorionic villi is associated with exaggerated production and elimina-

tion of prolan. Quantitative analysis of the prolan contents of the urine permits exact diagnosis.

The positive prolan findings in cases of chorionepithelioma led to further studies on tumors. These investigations showed that we were dealing with a quantitative hormone problem. In patients with tumors prolan elimination lies somewhere between the physiologic and the greatly increased levels of pregnancy. While in healthy women the normal output averages 5 mouse units to the liter, it rises in the pregnant to 1000 times this quantity, and in the presence of tumors the increase is only from 20 to 30 times that in the normal. These patients excrete approximately from 100 to 150 mouse units per liter of urine. To demonstrate these figures it is necessary to make use of the method of concentration (alcohol precipitation) which I have devised. It might be emphasized in this connection that the urine of carcinomatous patients will produce in the mouse practically only HVR I, very rarely II and III. This urine contains almost only follicle maturating hormone A. This phenomenon, however, is of no diagnostic value because the same reaction may be found in patients suffering from benign neoplasms. Nevertheless conditions are different in malignant newgrowths of the genitalia. While in benign genital tumors of women an increase of prolan A elimination is noticed in about 20 per cent of the cases, this incidence rises to 36 per cent in extragenital cancers and to 80 per cent in malignant genital neoplasms. Thus it is evident that the degree of hormone elimination is dependent not only upon the malignancy of the growth but also on its particular location. Naturally the question arose whether these hormonal changes are limited to genital carcinomas only in woman. Quantitative studies of prolan in the urine of men with carcinoma of the prostate yielded negative results. Studies made early in 1929 showed that the urine in a case of testicular carcinoma, contained both hormone A and B, exhibiting no difference therefore from that of a pregnant woman. Identical observations were reported by Fels and Matthias. Thus the fact is established that genital malignancy in man likewise creates special hormonal conditions. Omitting details I may state that the presence of the follicle maturation hormone (causing HVR I) in the urine of a man should arouse suspicion of a malignant testicular tumor. The reactions HVR II and III are of some value for the diagnosis of such malignancy, reactions which in women are characteristic for pregnancy. The factor which links these two phenomena to each other is that in most of the known cases, malignancy of the testicle was caused by a chorionepithelioma, though in rare instances also large celled seminomas of the testicle gave the same reaction. In two cases biologic proof of the presence of prolan in hydrocele fluid induced me to make a positive diagnosis of malignant neoplasm of the testicle, though the pathologist (Professor Anders) on the basis of histologic study was unable to make

this diagnosis, for cytologic examination of the puncture fluid did not show cells characteristic of malignancy. At least in these two cases the hormone-biologic test proved its superiority over the common cytologic search for typically malignant structures.

If implantation of very small particles of the suspected growth (0.05 to 0.1 gram) or injection of small amounts of tumor extract produces HVR II and III, then the diagnosis of malignancy can be made. This we succeeded in doing in instances of chorionepithelioma both in women and men.

These investigations have supplied the first foundations for a new procedure which I would designate as "Hormonal Tissue Diagnosis." Reactions initiated in an animal, consisting of follicular hemorrhages and luteinization, under certain conditions reveal the growth characteristics of implanted human tissue, that is, permit conclusions concerning its malignancy.

We may also mention briefly that prolan inhibits tumor growth (mouse carcinoma) so that in subsequent transplantations only little or no growth is noticed.

Finally I wish to call attention to a possible diagnostic value of increased elimination of follicle maturating hormones in the sexually mature woman. The hypophysis pours out these particular hormones at the time when function of the sexual gland ceases. Thus I found such increased elimination in the climacterium, the polyprolanic state. Operative removal of both ovaries in the mature woman is followed within two weeks by appearance of hormone A in the urine. If part of an ovary was intentionally preserved a hormonal test of the urine can later prove whether this rest is functionating or not. In examination of urines whose sources were unknown to me, I could isolate those from castrated women. I might mention that an increased prolan output was found in a young man three weeks after operative castration. It seems that this phenomenon in the human being represents a biologic law, making it possible to ascertain the activity or inactivity of the sex glands. In animals, conditions seemingly are different. While I could not find increased hormonal secretion in the urine of castrated mice and cattle, this was easily possible in the case of castrated rats and horses. How can this change in prolan production through castration be explained? (1) Prolan manifests its influences in the ovary. With removal of the ovary, prolan is deprived of its sphere of activity and thus uselessly produced it might leave the body by way of the secreted urine. (2) The sexual gland, as previously explained, can act as an inhibitor on the anterior lobe. With elimination of all such inhibition, one might assume, the anterior lobe will produce more hormones, which then find their way into the urine. This theory is supported by the discovery of Evans, confirmed by our observations, that the hypophysis of castrated animals actually contains more hormones. It is possible that both these

factors are actually at play after castration, that is to say, deprivation of the field for the activity of the follicle ripening hormones and removal of an inhibitor of hypophyseal hormone production by the sexual glands.

(For discussion, see page 932.)

SOME EXPERIENCES IN THE DIAGNOSIS AND TREATMENT OF CONGENITAL ANOMALIES OF THE FEMALE GENITAL TRACT*

BARTON COOKE HIRST, M.D., PHILADELPHIA, PA.

IF ONE could make an important announcement hitherto unknown, based on original research, he might face an audience of his colleagues with more assurance than I feel at present. But such an opportunity rarely falls to any one's lot. Or if he had long been engaged in an investigation with which his name had become associated he might always be heard with interest and advantage. Unfortunately I belong to neither class so that the choice of a subject that might be worth your attention is difficult. The difficulty is increased by what seems to be a temporary pause in the surprising advance of recent years. Even the endocrinology of the menstrual cycle, the latest subject of intensive study appears to have approached a conclusion with Lepine's announcement of his separation of Prolan A from Prolan B, and with the practice now being adopted of providing oneself with the sex hormone for therapeutic use from the urine of one's own pregnant patients, thus dispensing with commercial products, and obtaining a more accurate dosage.

In doubt as to what to talk about, it occurred to me, in reviewing a long medical career, to ask myself in what class of cases there had been the greatest difficulty in diagnosis, the greatest difficulty in selecting off hand the appropriate treatment and the least help in medical literature for standardizing our conduct. Any student of gynecology, it seems to me, in propounding such a question to himself must find the answer in congenital anomalies of development in the female genital tract. They are all described in comprehensive treatises on gynecology, it is true, but little is to be found anywhere on the vagaries of their presentation in individual cases, nor of the treatment of bizarre examples not at all conforming to the usual types. Hence an excursion into medical casuistry may be forgiven in the study of these conditions, although the mere recital of cases is usually tedious and unprofitable. But after all, what is experience but the sum of individual cases.

An alternative subject appealing to me is the curious appearance of cancer in the pelvic and adjoining bones during the puerperium seen

*Read at a meeting of the Brooklyn Gynecological Society, April 1, 1932.

lately as a metastasis from an unsuspected primary growth, manifesting itself in a total inability to rise from bed or to walk, and regarded as hysteria. Another possibility was an analysis of hundreds of temperature charts, substantiating the claim in favor of the active treatment of septic abortions.

The selfish motive, however, of acquiring additional vicarious experience by listening to observations of congenital anomalies made by the members of the Society, dictated the choice of the subject of this communication.

As an example of the obscurity of some of these developmental anomalies in the female genital tract, how would one interpret the following symptoms, history, and physical findings?

A young nullipara seized with chills, fever, and abdominal pain was operated upon two and one-half years ago by a general surgeon for appendicitis. No acute appendicitis was found. A few weeks after returning from the hospital, coincident with a period, chills and fever returned and for the first time the urine was described by the patient as having a black color, with particles of solid matter in it. This phenomenon recurred with each period for the next six months, the discolored urine appearing usually a few days before or after the period, always with considerable fever, and at no other time in the month. She was returned to the gynecologic department of the general hospital in which she had been operated upon for a study, continued for six weeks, including repeated examinations: cystoscopy, pyelography, microscopic examination of catheterized and normally evacuated urine. The latter had a few blood cells and pus in it, the former contained none. The patient was finally discharged without a diagnosis.

Entering my service in the Graduate Hospital all these examinations were repeated without result, and the patient was about to be discharged as a malingerer when one day just before an expected period, in a final examination, a queer material was noticed on the glove of the examining hand: semisolid, dark brown in color, looking almost like dehydrated, decomposing blood. A closer investigation showed this material was oozing from the external urinary meatus and that its origin was from a distended pouch alongside the urethra. On opening the latter a considerable quantity of the dark colored material was expressed. Investigating the depth of the sac a uterine sound passed into a sinus some four inches or more upward and to the left. Suspecting a possible endometrial implant, the abdomen was opened and the pelvis searched for a possible endometriosis, but none was found. In a cursory examination of the pelvic organs themselves, they appeared to be normal. The sac in the neighborhood of the urethra and communicating with it was dissected out. The sinus extending upward and outward was curetted with a small, sharp curette. The patient reappeared seven months later reporting that there was no more fever with the periods, that the dark discoloration of the urine had ceased but that with each period a day or two before or afterward there was a discharge of bright blood independent of the period itself.

Reporting a year later all symptoms had disappeared and the patient had no discomfort. An examination showed a hollow space where the sac had been and the sinus had closed.

Speculating on the possible explanation of an unusual train of symptoms, which had interested me at the time but had been forgotten, it seemed possible that there had been a rudimentary development of the left müllerian duct as far at least as the uterine cavity and vagina were

concerned; possibly a condition analogous to a uterus bicornis rudimentarius solidus on one side, or perhaps a duplicity in the canalization of one müllerian duct, which has been noted. A uterograph was taken at this time, showing a typical picture of uterus unicornis.

Why there were no symptoms in this case until she had reached the age of twenty-five is inexplicable. Whether the appearance of the anomalous menstruation had anything to do with the appendectomy is difficult to say, but probably not. At any rate the treatment proved satisfactory, although adopted in haphazard fashion without adequate knowledge of the true condition. In fact the explanation just offered might be criticized as little more than a surmise. Nevertheless it is the only one I can think of. Here is another clinical puzzle.

A young nullipara, married a year, twenty-one years of age, was brought to the University Hospital with an acute abdominal condition thought by her physician in the country to be a ruptured ectopic pregnancy. She had begun to menstruate at the age of fifteen and the periods had been regular ever since; there was no missed period. She had been seized with severe abdominal pain at the time of an expected period. Her physician found an abdominal enlargement as great as that of a six months' pregnancy, very sensitive on pressure. The patient seemed shocked.

In my examination the vagina readily admitted two fingers: the cervix could not be reached. There was a tumor bulging the right lateral vaginal wall and vault, apparently continuous with the abdominal tumor reaching to the navel, firm in consistency and surrounded laterally and above by a corona of resonance. There were no symptoms of internal hemorrhage, no signs of pregnancy. But on account of the patient's acute suffering and some symptoms of shock an immediate section was done. There was difficulty in opening the peritoneal cavity as the anterior peritoneal reduplication was lifted to the level of the navel, but on entering the abdominal cavity an explanation of the unusual symptoms was found in a complete uterus didelphys perched on the top of an enormous hematocolpos in one atresic half of the double vagina in which the menstrual blood from one of the uterine bodies had accumulated for six years. There was no hematometra nor hematosalpinx. The other half of the vagina, perfectly patent, communicated with the left half of the double uterus. Hence the apparently normal menstruation.

An incision was made in the right vaginal wall below the peritoneal reduplication and a counter opening made just within the vulva. Both openings were drained with a large caliber stiffwalled rubber tube. The accumulated menstrual blood was thoroughly washed out. The upper tube was removed after a few days. The lower tube remained for some time to secure permanent patency of the atresic vagina which was found to be maintained a year later.

The father of the girl, a physician present in the operating room during the operation, asked what the prospects were should his daughter become pregnant. The two uterine halves were distinctly infantile in development, so I expressed the belief that pregnancy would terminate probably in an early miscarriage or possibly in rupture. At his urgent request therefore I sterilized her by double salpingectomy and the removal of the interstitial portion of the tube by exsecting both cornua. Curiously enough she reported a year later that she had never menstruated since, though both ovaries remained and very little if any endometrium was removed by the exsection of the cornua. Otherwise she had nothing to complain of.

One more case will serve the purpose of emphasizing the ever present possibility of these aberrant anomalies, confusing the diagnosis and making difficult the immediate choice of an appropriate treatment.

A young girl, aged thirteen, had begun to menstruate nine months before. The periods were normal. Four months after the establishment of menstruation she applied to the dispensary of physicotherapy for the diathermic treatment of specific endocervicitis. In the course of the treatment pain was complained of on the left side so she was referred to me to see if there was any tubal involvement. Finding a firm, spherical or fusiform mass at the site of the left tube, which however was not adherent, I believed the child had a small dermoid cyst and recommended operation. On opening the abdomen a perfect uterus bicornis was discovered with wide separation of the horns and the intervening uterine structure in the shape of a uterus incudiformis. The tubes and ovaries on both sides were normal. During the child's previous treatment a slight tumefaction in the left vaginal wall and fornix was noticed but no attention was paid to it.

Two months later the child returned with increased pain on the left side and was then found to have an unmistakable cystic tumor occupying the left vaginal fornix, the upper part of the left vaginal wall and reaching three fingerbreadths above Poupart's ligament, apparently extending into the abdominal cavity. It was regarded naturally as an intraligamentary cyst. The abdomen was again opened but the cyst was below the pelvic diaphragm and could not be approached through the abdominal cavity. Besides it was in such close relation with the bladder that it appeared to be possibly a vesical sacculation. Distending the bladder with water the differentiation between the two was still more difficult. Again the abdomen was closed without doing anything. During the convalescence from the section the vaginal tumor was tapped with a long needle, its contents withdrawn by a piston syringe, proved to be pus with pure culture of Staphylococcus albus. Then both bladder and tumor cavity were filled with sodium iodide and an x-ray picture taken. It proved that an air distention of the bladder and sodium iodide distention of the cyst cavity would have made a better picture, but the differentiation between the two cavities was plainly established. A large opening was made into the cyst. Cyst wall and vaginal wall were sewed together and the cavity drained with a large caliber tube. The final follow up examination showed the inner cyst wall flush with the vaginal wall and clothed with vaginal epithelium.

Pretty certainly this was an unusually large cyst of Gärtner's duct extending higher into the base of the broad ligament than usual. As is well known, the persistence of the wolffian duct is twice as frequent in duplicity of the genital tract as in a perfectly fused and single genital tract. How it became infected is a mystery. Curiously enough at no time had the patient any rise of temperature whatever.

Without a tedious citation of other obscure cases of developmental anomalies to sustain the contention that we must be prepared to meet conditions under this head baffling the first attempt at diagnosis, in addition to many easily recognized off hand, allow me to present briefly another interesting phase of the subject, namely, What should be the ultimate collective judgment of the profession as to the propriety of some of the methods of treatment proposed, in regard to which there is at present difference of opinion.

Passing with a mere mention such obviously indicated procedures in one's practice as converting two uterine cavities into one by splitting the septum of a septate uterus, treating similarly a double vagina, uniting the cervix of a uterus unicornis with a huge hematometra to an artificially constructed vagina and so on, it would interest me greatly

to hear the views of the members present on certain moot questions in the treatment of absent vagina and uterus. I confess to a prejudice against using a segment of intestine or rectum by an operation attended with some risk, merely to permit coitus: but it must be owned that the other proposals to establish an artificial canal for that purpose have been usually unsatisfactory. I have tried most of them, I think, including implanting the vagina from one woman into another. In the last mentioned case the woman with the implanted vagina left the hospital in two weeks with a canal lined with mucous membrane, admitting the full length of a bivalve speculum of considerable size. But a sufficiently long continued follow up observation of these cases usually shows, I think, shrinkage both in length and breadth of the artificial canal. What I had particularly in mind to ask is, in those cases of absent vagina and uterus encountered occasionally, in which coitus is practiced by the urethra, after prolonged and gradual dilatation, without apparent harm to the woman, should she be allowed to continue that practice? I recall a case in which a two-finger examination through the urethra was easily practicable. The married couple, having lived together some years, were unaware of any anatomic peculiarity. Their sexual relations were said to be satisfactory. The woman came to me for sterility. She was a poor surgical risk and did so badly in an attempt to utilize a segment of the rectum for an artificial vagina that the operation was given up. She refused further surgical intervention. Meanwhile a cystoscopy showed no disease of the bladder and there was no incontinence of urine. The patient disappeared and I have no means of learning her subsequent history. I have often wondered if in such cases injury and infection of the bladder could be indefinitely avoided and, if that were so, whether we would be justified in letting well enough alone.

One must be prepared for some ethical questions in these cases of absent vagina and uterus that are not so easily answered.

A young girl, perfectly formed in other respects, but with no uterus or vagina, and about to be engaged to an eligible young man, was brought by her mother who asked first whether it was possible to correct the congenital defect, and secondly, whether the prospective fiance should be informed of the girl's condition. To the first question a negative reply would be given by most of us, I think, in the case of a young woman for whom married life would not begin for a number of months. The second question was hardly fair to put to a physician for a medical opinion, but as a matter of ethics alone there could, it would seem, be only one answer. A colleague however differed from me and the girl was operated upon. As a social as well as a medical problem it would have been interesting to learn the result, but I had no means of doing so.

In contrast with this controversial subject of absence of the lower genital tract it is a relief to turn to another congenital defect in the female, anus vestibularis incorrectly so-called, for as we all know the anus in these cases is in the fossa navicularis. Very few physicians can

have much experience in handling this defect for it is rare. The combined statistics of Von Bardeleben and Stoeckel show only one for each in 63,000 births. Fortunately the diagnosis is unmistakable and the treatment is easy, safe and the result usually satisfactory. I happen to have operated upon a young child and a young girl with this condition. By a fairly deep median perineal incision, a circular incision around the anus to mobilize it, with care to make the lateral incision somewhat superficial to avoid the anal nerves so as to preserve continence, the anus is pushed back to its normal position and the perineal incision closed in front of it.

Even the most superficial review of congenital defects, such as this necessarily is, would be incomplete without some reference to their effect on childbirth. There is not so much to be said on this part of the subject for many of these defects preclude conception, and professional opinion is pretty well in accord as to their management in parturition. For a most excellent statistical, clinical, and historic study of duplicity of the genital tract in pregnancy and childbirth one could not do better than to consult the analysis of 35 cases among 141,946 childbearing women in the report of the Lying-In Hospital of New York of March, 1932. With one of the conclusions in this paper I am in hearty agreement. "The necessity for operative correction has been greatly exaggerated."

Some years ago two cases of cesarean section for labor in a double uterus were reported, at a meeting of the American Gynecological Society, and I regret to remember that in the discussion I added two more for I am not at all sure they were necessary. It is the bulk of the nonpregnant uterus that is usually regarded as an insuperable obstacle demanding section, but we have all seen natural labors in these cases. There is little difficulty in the diagnosis except perhaps by the inexperienced. I recall an amusing consultation in which a general practitioner was doubtful of his sanity, for on one examination he found a rapidly progressing labor and on another all signs of progress had disappeared.

It must not be assumed, however, that all these cases may be regarded with indifference. The incidence of legitimate indications for operation is high, as is that of numerous complications and in some cases unexpected difficulties are encountered in conditions that appear easily manageable. As an example I recall a transverse fetal position in a uterus incudiformis, the interior of which more closely resembled a uterus bicornis, which is often the case. A version appeared perfectly practicable but the head was so impacted in one horn and the shoulder in the other that the fetus could not be budged and a cesarean section was necessary with the added danger of a precedent intrauterine manipulation.

1821 Spruce Street.

(For discussion, see page 947.)

AVERTIN ANALGESIA IN OBSTETRICS

A Report of One Hundred and Fifty Cases*

George G. Cochran, Jr., B.S., M.D., F.A.C.S., Brooklyn, N. Y.

(From the Department of Obstetrics and Gynecology, The Brooklyn Hospital)

IN ORDER to evaluate the effectiveness of "avertin" or tribromethyl alcohol as an analgesic agent during labor, a study of one hundred and fifty cases was made on the obstetric service of The Brooklyn Hospital. The anesthetic properties of this drug were demonstrated by Eichholtz[1] in 1927. During the past four years, it has been widely used, especially in Germany, as a basal anesthetic for surgical operations, and numerous clinical and experimental studies concerning it have appeared. Very little work comparatively, has been done in its use as an analgesic agent for the parturient woman.

H. J. Stander,[2] following his studies on avertin in dosage amounting to 100 mg. of drug per kilogram of body weight, found no changes in blood chemistry in the nonprotein nitrogen, urea nitrogen, uric acid, lactic acid, creatinin, chlorides, or carbon dioxide combining power, and only a very slight increase in blood sugar. However, in view of the manner in which avertin is detoxicated in the liver,[3] it does not seem advisable to use it in such conditions as eclampsia, in which liver injury is an outstanding factor.

Stander, however, observed no evidence of liver necrosis in dogs, when a dose of 500 mg. per kilogram was used. Bearing this in mind, it was decided in the study of avertin to use the drug in no patient giving evidence of toxemia.

Dosage.—The dangers have been fully enumerated by a number of German surgeons[4] who pioneered in its use, and there can be no doubt that their mortality rate has been due to overdosage, which in turn has been due to the effort to induce anesthesia with avertin unsupported. This is neither necessary nor advisable. Once given avertin is rapidly absorbed, and beyond control. To obtain the best results with safety, an average dose should be given, and any remaining deficit in the anesthesia of the second stage of labor should be made up by nitrous oxide and oxygen inhalation. Also, in some cases of cesarean section when an inhalation anesthetic is to be avoided, local anesthesia may be the supplement of choice. Other factors also enter the problem of dosage for the parturient woman, such as the effect of the drug on the baby, the uterine contraction, length of labor, and so on.

Our first attempts were made with one-half the surgical dose, or 50 mg. per kilogram. This was later increased to 60, then 80. In one of our three cesarean cases 100 mg. per kilogram was used.

---

*Read at a meeting of the Brooklyn Gynecological Society, April 1, 1932.

Administration.—No attempt was made to select the patients. As soon as labor was definitely established with regular pains, and beginning dilatation of the cervix, two procedures were tried; one with a preliminary hypodermic injection of morphine and scopolamine, the other without these. The result in general seemed better with the first plan, so that the routine finally adopted is: Morphine gr. 1/8, scopolamine gr. 1/200, hypodermically, which is repeated at about two-hour intervals until the cervix is effaced, and dilatation has progressed to about one inch. At this time a 60 mg. per kilogram dose of avertin is administered into the rectum, with the caution of introducing the catheter above the presenting part if it happens to be in the cavity of the pelvis, and starting the injection immediately after the cessation of a uterine contraction. This precaution usually insures against expulsion of the drug, as the absorption of the drug is very rapid, and even though the water vehicle may be subsequently expelled, the desired effect of the drug is obtained.

The state of amnesia is usually maintained from two to four hours, while the analgesia is prolonged to six or eight hours in varying degree. After three hours the dose is repeated without hesitation. The intention is to give the second dose just before the beginning of the second stage. In two cases of long labor a third dose was used.

Successful amnesia and analgesia is obtained with any agent only by constant and thoughtful observation of the progress of labor. No two cases are exactly alike, but with the skill acquired by the observation of many cases, complete amnesia and analgesia can be obtained in the majority of cases. When failures occurred, it was the result of inaccurate observation of the progress of labor, or timidity as to the use of sufficient amount of the drug.

Action.—An excellent result was obtained with 60 mg. dose. With the 80 mg. amount there was noted diminution in the strength of the contractions of the uterus, a longer interval between pains, and a consequent prolongation of the labor. With the smaller dose of 50 mg., insufficient analgesia and amnesia were obtained. On the average, the action of the drug was manifested in fifteen minutes. The patients became drowsy, slept through pains, and were oblivious to their surroundings. Many of them do not remember being transported from the labor room to the delivery room. The general condition of the women was excellent. No cyanosis was noted. There was no noticeable change in pulse or respiration. Dandy[5] and White[6] using 100 mg. per kilogram, reported a distinct fall in blood pressure. In this series of cases using a smaller dose, no appreciable drop was recorded. A few of the cases were quite irrational. The resultant restlessness often required additional nursing. The fluid intake and output was normal. There was no evidence of rectal irritation.

Labor.—In this series, five-sixths of the patients were primiparae,

but no prolongation of labor was noted. The average duration was: primiparae: first stage, fourteen hours, (the longest, fifty-eight hours, shortest, four hours). Second stage, one hour and ten minutes. Multiparae: first stage, seven hours. Second stage, twenty minutes. Brown[8] reporting on the use of pernocton in one hundred and thirty cases, records the average length of labor as eighteen hours.

Hamblin and Hamblin[9] in their paper on "The Oral Administration of Sodium Amytal," in 50 cases noticed no prolongation of labor, as their average length of labor for primiparae was fourteen hours. Schoeneck[10] using Gwathmey ether in oil routine, in two hundred and forty-five cases at The Brooklyn Hospital, found the average first stage of labor to be fourteen hours. It would seem that avertin compares favorably with these other agents, in that labor is not prolonged, and the efficiency of the uterine contraction is not decreased. However, it was noticed that shortly after the administration of the drug, the interval between pains was lengthened for a short time.

Delivery.—The presenting part was noted in 117 cases as a vertex with the occiput anterior; in 26 cases as occiput posterior, and in 7 cases as a breech.

The method of delivery was, cesarean section 3; high forceps 1; low forceps 12; forceps control and perineotomy 101; spontaneous vertex 26; spontaneous breech 3; breech extraction 4. With the high incidence of forceps control it is rather hard to judge the duration of the second stage. We are of the impression that in a number of cases there was a definite retardation of the progress of labor in the second stage. The contributing factors were a diminution in the strength of contractions, increased interval between expulsive pains, and the depth of analgesia, with its loss of cooperation.

Many individuals obeyed instructions to bear down, yet on questioning the next day failed to remember their experience in the delivery room. In general the patients were quiet and easily managed.

The amount of anesthetic was greatly reduced. Except in a few incidences a supplemental inhalation of nitrous oxide and oxygen was given at the time of actual delivery and for perineal repair. In 10 cases delivery was accomplished without the use of inhalation anesthesia.

Avertin is a great aid as a basal anesthetic in the performance of cesarean section operation. We used the 80 mg. dose, supplemented by nitrous oxide and oxygen in two cases, and local anesthesia in the third case.

Babies.—Six of the babies required resuscitation. The others showed no evidence of cyanosis or narcosis, each breathing and crying vigorously immediately after birth. There were 4 stillbirths.

Analyzing the stillbirths, only one could possibly be attributed to avertin. The first case was a breech presentation; the patient was admitted to the hospital with a prolapsed pulseless cord. The second was a syphilitic patient, and on admission

no fetal heart was heard. The third was a primipara who had a fifty-eight-hour labor and was brought to the hospital after being in labor forty-five hours at home. Examination revealed a complicating undilated cervix, bronchopneumonia, foul amniotic fluid, and a persistent occipitoposterior position. Her condition on admission was recorded as serious. After complete rest with morphine and bromide and chloral per rectum, labor advanced to full dilatation of the cervix. About twenty minutes before delivery a 100 mg. dose of avertin was given, and supplemented by a small amount of nitrous oxide and oxygen. The fetus was delivered with axis-traction forceps, and the patient later recovered and was discharged from the hospital. We feel that this case was a real indication for the use of avertin.

The fourth stillbirth was a premature infant weighing five pounds. Avertin was given one hour before delivery. The patient experienced a very rapid second stage, with exceedingly hard contractions. The delivery was spontaneous. Immediately following its birth, the baby took several gasps, but all means of resuscitation failed. Autopsy was refused. We are in doubt as to whether this was an avertin death or the result of prematurity, cerebral hemorrhage, or atelectasis.

Results.—The results of our experiences with these 150 cases were tabulated after the method of the Boston Lying-In Hospital.

Of the 32 cases receiving two doses of avertin: 5 remember clearly; 15 remember vaguely, and 17 remember nothing concerning their labor. Two cases receiving 3 doses remember vaguely. One hundred and fifteen cases received one dose: 20 of these remember clearly, 65 remember nothing, and 30 vaguely remember their experiences.

Of the 25 who remember clearly, 20 said they had a hard or moderately hard time. The other 5 said they had an easy time, and that they had received considerable relief from the medication.

CONCLUSIONS

1. Avertin is apparently a safe analgesic agent.
2. The best results were obtained with a 60 mg. per kilogram dose.
3. Its use does not prolong labor or increase the incidence of operative delivery.
4. Avertin produces a successful state of analgesia or amnesia in the majority of cases.

REFERENCES

(1) *Eichholtz, F.:* Deutsche med. Wchnschr. **53**: 710, 1927. (2) *Stander, H. J.:* Am. J. Obst. & Gynec. **22**: 219, 1931. (3) *Endoh, C.:* Biochem. Ztschr. **152**: 276, 1924. (4) *Schwalbe, J.:* Deutsche med. Wchnschr. **53**: 2064, 1927; **54**: 558, 1928. (5) *Dandy, W. E.:* J. A. M. A. **26**: 1860, 1931. (6) *White, Chas. S.:* Surg. Gynec. Obst. **51**: 361, 1930. (8) *Brown, R.:* Am. J. Obst. & Gynec. **22**: 219, 1931. (9) *Hamblin, E. C., and Hamblin, D. O.:* Am. J. Obst. & Gynec. **21**: 715, 1931. (10) *Schoeneck, F.:* Personal Communication.

429 Clinton Avenue.

(For discussion, see page 947.)

FETAL MORTALITY AND BREECH PRESENTATION

DANIEL GREEN MORTON, M.D., SAN FRANCISCO, CALIF.

(From the Department of Obstetrics and Gynecology, University of California Medical School)

NO STUDY which inquires into the results of a condition leading to a 10 per cent to 15 per cent fetal mortality requires justification. Bad results in cases of breech presentation are too apt to be ascribed to a more or less unavoidable condition and, as such, viewed complacently. That such complacency is not due to negligence but rather to the fact that the defects in our management of cases of breech presentation are not glaring and are therefore difficult to combat, is apparent. Impressed by the high fetal mortality in breech presentation, I have made a critical study of the 301 breech deliveries that occurred in 8509 deliveries in the University of California Hospital. I feel that this study has brought out a number of facts which should aid us to improve materially our treatment and that they are, therefore, worth recording.

Incidence.—The 301 breech presentations constitute 3.53 per cent of the 8509 deliveries, a percentage that corresponds closely with those reported in other series. Since 16 of these breech presentations occurred in women delivered by cesarean section and presented no problem of delivery, they are not included in the calculations for fetal mortality, etc. The exclusion of the 16 cases leaves 285 for consideration, of which 125 occurred in multiparae and 160 in primiparae. Authorities are generally agreed that breech presentation is more common in the multipara than in the primipara but, curiously enough, the incidence in this series was 3.9 per cent for primiparae and only 2.8 per cent for multiparae.

Viability.—Not all babies delivered by breech were viable, and there were some babies which were dead on admission to the hospital. By viable, we mean arbitrarily all babies weighing 1500 gm. or more which were living when the patient was admitted to the hospital, in the absence of marked abnormalities incompatible with life, such as spina bifida, hydrocephalus, etc. Of the 285, 256 were viable, 29 dead or nonviable, as shown in Table I.

TABLE I. FETAL VIABILITY

	TOTAL CASES	DEAD OR NONVIABLE FETUS	VIABLE FETUS
Primipara	160	12	148
Multipara	125	17	108
Total	285	29	256

Weight of Babies and Duration of Labor.—The average weight of 228 viable babies was 3144.4 gm., 300 gm. less than the average for the clinic. The largest baby weighed 5075 gm. The average length of labor was 10.59 hours for multiparae, and 16.41 hours for primiparae, both slightly less than the averages commonly stated in textbooks.

Fetal Position.—The exact positions and their frequencies are tabulated in Table II, on the basis of the total 301 cases. They require no comment.

TABLE II. POSITION

POSITION	TIMES	PER CENT
L.S.A.	134	44.5
R.S.A.	89	29.5
R.S.P.	39	12.5
L.S.P.	26	8.6
Undifferentiated	13	4.9
Total	301	100.

In 278 cases mention was made whether the child presented as frank breech, etc. Frank breech occurred 187 times or 67.3 per cent; footling breech occurred 75 times or 26.9 per cent; complete breech occurred 16 times or 5.8 per cent.

Diagnosis and Conversion.—In 118 of the 285, or almost one-half of the cases, a diagnosis of vertex presentation was made at the last outpatient clinic visit before delivery. Whether these figures represent a true state of affairs or not is difficult to say: often the patients did not return when requested, and this last clinic visit occasionally was even one month prior to delivery: moreover, fourth year students occasionally made the last abdominal examination on patients who had been coming regularly to the clinic and who had previously been found to be normal. In an additional 63 cases, no diagnosis was made, usually because the patient was not seen until late in labor. In 104 cases a diagnosis of breech presentation was made prenatally, and an attempt was made to convert 20 of these to vertex. The attempt proved futile in 16, and in the remaining four the breech presentation recurred. Unfortunately, a perusal of the prenatal records of the entire 8509 cases would be necessary to determine the number of cases in which conversion to vertex presentation was successful and permanent. That conversion of a breech to a vertex presentation is worth while is undeniable, since fetal mortality in vertex presentation is so much less than in breech, and the chance of harming the fetus in performing the maneuver is exceedingly slight. However, in a large proportion of cases, the diagnosis of breech presentation is so confusing or the presentation occurs so late in pregnancy that the question of conversion either does not arise at all, or the maneuver becomes actually impossible by the time the diagnosis is made. These facts make of it a method of treatment which we may or may not be able to use, but one on which we can never depend.

Fetal Mortality.—Of the 256 viable babies, 24 were stillborn, and 14 died in the hospital between ten and fourteen days after delivery, making the total mortality 38, or 14.8 per cent. Of the 38 dead babies, 20 were fullterm (weighing over 2500 gm.), and 18 were premature (1500 to 2500 gm.). The distribution between multiparae and primiparae, term and premature, etc., is shown in Table III.

TABLE III. FETAL MORTALITY

VIABLE	STILLBORN		DYING IN HOSPITAL		TOTAL	PER CENT
	TERM.	PREM.	TERM.	PREM.		
Multipara 108 cases	6	3	0	7	16	14.8
Primipara 148 cases	12	3	2	5	22	14.8
256 cases	18	6	2	12	38	14.8

Two facts stand out clearly: (1) that breech delivery was rarely, if ever, responsible for stillbirth in the premature cases, and (2) that fetal stillbirth at term was almost invariably associated with birth trauma. This is shown by the following. Of the 18 premature fetal deaths, 12 occurred *after* birth, mostly with such diagnoses as prematurity, aspirative pneumonia, respiratory failure. Of the 6 stillborn, in no case was there difficulty with the delivery sufficient to explain the death. Moreover, three occurred in multiparae and 3 in primiparae. On the other hand, of the 20 fetal deaths at term, 18 were stillborn, and only two occurred later, one of these from an intracranial hemorrhage. In short, 19 of the 20 fetal deaths at term were definitely associated with birth trauma. Further testimony to this fact is that 14 of the 20 fetal deaths at term occurred in primiparae, in which one would expect to have more difficulty with the delivery.

Following this line of thought, if we separate the pregnancies at fullterm from those premature, we get the amazing figures shown in Table IV.

TABLE IV. FETAL MORTALITY AT TERM

VIABLE		STILLBORN	MORTALITY
At term	219 cases	20	9.10%
Premature	37 cases	18	48.6 %
Total	256 cases	38	14.8 %

From this table it would appear that a breech position carries an extraordinarily bad prognosis for a premature child. However, an analysis of the cases discloses no reason for the high mortality since there was no difficulty encountered in delivering any of the premature infants in a breech position. On the other hand, I found upon reviewing the premature fetal mortality for several years for all presentations, in-

cluding those dying in the hospital as well as those stillborn, that 88 died of the 239 premature babies, or 36.8 per cent. The difference between the figures 36.8 per cent and 48.6 per cent is 12 per cent which I feel represents the additional risk for prematures delivered by breech. It is gratifying, moreover, to find after excluding the premature cases that the fetal mortality in viable fullterm cases is but 9.1 per cent. Realizing that the prognosis for prematures is bad at best, and having learned that the majority of the premature deaths occur after delivery and apparently unassociated with it, we naturally feel less responsibility for them than for those occurring at term. The histories give no clue as to why these women fell into labor prematurely.

Analysis of the fetal deaths with respect to position revealed no significant association. The various positions were present in the fetal death group in about the same proportion as those cited for the entire series. In this group, frank breech occurred in 63.8 per cent, footling breech in 33.3 per cent, and complete breech in 2.9 per cent, figures which also tally closely with those for the complete series. Likewise, the divisions into term and premature, actual stillbirths and neonatal deaths, retained proportions closely parallel to those stated for the total number of cases. Apparently fetal mortality in breech presentation is uninfluenced by position.

Mode of Delivery.—In an effort to ascertain the reasons for fetal mortality, the various modes of delivery are tabulated, together with their accompanying mortalities, in Table V.

TABLE V. MODE OF DELIVERY

TYPE OF DELIVERY	TIMES	FETUS ALIVE	STILLBORN			FETAL MORTALITY PER CENT
			TERM	PREMATURE	TOTAL	
1. Spontaneous	15	8	1	6	7	46.6
2. Breech extraction Mauriceau	219	191	16	12	28	12.7
3. Forceps on aftercoming head	20	17	3	0	3	15.0
4. Forceps on breech	2	2	0	0	0	00.
Total*	256	218	20	18	38	14.8

*Omitting dead and nonviable fetuses.

The following points deserve comment: (1) regarding the actual mode of delivery: other methods than breech extraction followed by the Mauriceau maneuver, the usual mode in this clinic, were not employed sufficiently often to justify comparison with it; (2) in the spontaneous cases over which we have little if any control, there was a high fetal mortality for which the obstetrician was not actually responsible. Three of

the stillborn prematures in this group were not actually stillborn but died later in the hospital. The one fullterm stillborn was due to an accident: the woman called the hospital too late in labor for the physician to arrive in time for the delivery. Upon arrival, he found the baby born, except for the head which had remained in the vagina for some fifteen minutes, without either the patient or her husband making an effort to extract it; (3) in Group 2, eight of the 28 total stillborn or almost one third, occurred in cases in which labor had been induced (six by bag). Eight, or two-thirds, of the 12 stillborn prematures were babies which died in the hospital after delivery; (4) in Group 3, two of the three fetal deaths occurred before we used the Piper forceps, and the operation was attempted rather as a last resort after ordinary methods of extraction had proved exceedingly difficult; (5) in Group 4, the operation was done once accidentally, the presentation having been mistaken for a vertex, and once purposely, in place of a fillet.

If we rearrange the table to exclude the prematures, we gain a clearer idea of the mortality for which the obstetrician may have been responsible and upon which we should be able to improve.

From a perusal of this table the inference is that, barring accidents and interference, the fetal results were relatively good; moreover, that bad results were not distinctly related to the actual method of delivery but were definitely related to efforts to induce and complete labor.

TABLE VI. MODE OF DELIVERY (EXCLUDING PREMATURES)

DELIVERY	VIABLE-TERM	STILL-BORN	MORTALITY PER CENT	COMMENT AS TO FETAL DEATH
Spontaneous	8	1	12.5	An accident
Breech extraction	192	16	8.3	Six after induced labor (five by bag). Manual dilatation completing the cervical dilatation in 4 of the 5 cases
Forceps on aftercoming head	18	3	16.6	Two of the three as last resort with ordinary forceps
Forceps on breech	1	0	0.0	On purpose in frank breech in place of fillet
Total	219	20	9.1	

ANALYSIS OF DIFFICULTIES

Induction of labor, completing the dilatation of the cervix manually, and breaking up the breech at full cervical dilatation were three activities which appear to have been followed by disastrous consequences. Let us first indict and then excuse them for, of course, they had their indications and were tried usually in the cases which presented real obstetric problems.

Induction of Labor.—Labor was induced in 25 women of the 285, 21 of

which were carrying viable babies. Of the 21, seven babies, or one-third were stillborn (five at term, two premature). Table VII shows that sound justification is needed for a procedure which results in a 33.3 per cent fetal mortality. Obviously, the bag is largely responsible for this excessively high mortality.

TABLE VII. INDUCTION OF LABOR

METHOD	TIMES	ALIVE		STILLBORN		NON-VIABLE	MORTALITY PER CENT
		TERM	PREMATURE	TERM	PREMATURE		
1. Castor oil and quinine	9	8	0	1	0	0	11.1
2. Hydrostatic bag	11	0	1	4	2	4	85.7
3. Castor oil and quinine, rupture membranes, nasal pituitrin	5	4	1	0	0	0	0.0
Total	25	12	2	5	2	4	33.3

The indications for inducing labor in those women are tabulated in Table VIII.

TABLE VIII. INDICATIONS FOR INDUCTION OF LABOR

INDICATION	TIMES	ALIVE		STILLBORN		NON-VIABLE
		TERM	PREMATURE	TERM	PREMATURE	
1. Toxemia	5	1	0	0	1	3
2. Past term	4	3	0	1	0	0
3. Premature rupture of membranes	5	3	1	0	0	1
4. Pelvic contraction	1	0	0	0	1	0
5. Questionable or unknown indication	5	1	0	4	0	0
6. Experimental method of induction	5	4	1	0	0	0
Total	25	12	2	5	2	4

17 viable term babies, 5 stillborn (4 after bag, 1 after castor oil and quinine)
4 viable premature, 2 stillborn (both after bag)

In Groups 1 and 2, the indications are perfectly justifiable with two stillborn babies out of six viable. The average weight of the past term babies was 4120 gm. Groups 3 and 4 are open to question as justifiable indications, with one stillborn baby out of five viable. Group 5 should not have been induced; the indications for three of the cases were, (a)

two days overterm (baby weighed 8.2 pounds), (b) eight days past term (no weight, baby measured 48 cm. long), (c) "slight toxemia, two weeks premature" (the toxemia consisted of a mild elevation in blood pressure without other signs or symptoms). In the two remaining cases, no indications could be found. In this group there were five viable babies of which four were born dead.

Manual Dilatation of the Cervix.—In six cases, some degree of manual dilatation of the cervix was carried out (usually to complete dilatation of the cervix, already 6, 7, or 8 cm. dilated). Four, or two-thirds of the babies were stillborn. All these women were at term. Four of the six labors were induced, twice by castor oil and quinine, and twice by hydrostatic bag, a further indictment of the induction of labor. Three of the induced labors resulted in stillborn babies. The reasons for the manual dilatations are tabulated in Table IX.

TABLE IX. REASONS FOR COMPLETING THE DILATATION OF THE CERVIX MANUALLY

REASON	TIMES	RESULT
Poor pains	3	One stillborn (1 after bag, 1 after castor oil and quinine, 1 spontaneous)
Fetal distress	2	Two stillborn (1 after castor oil and quinine, 1 spontaneous)
Maternal distress	1	One stillborn (after bag)
Times	6	Stillborn 4

The average length of labor in this group was 31.13 hours, the longest being 48 hours, showing, as justification for manual dilatation, that these cases presented a problem, any solution of which might have been incorrect.

Breaking Up the Breech at Full Dilatation.—Although this procedure is recommended as a routine by some, the contention being that it gives the obstetrician a leg to pull on if it becomes necessary to extract the child in a hurry, I feel that it is an unusually bad thing to do. This procedure was deemed necessary five times and three of the babies were delivered stillborn. The reasons are presented in Table X.

TABLE X. BREECH BROKEN UP AT FULL DILATATION

REASON	TIMES	RESULTS
Poor pains	3	Two stillborn (1 after bag)
Contracted pelvis	1	One stillborn
No reason given	1	Alive
Times	5	Stillborn 3

The average length of labor was 22.1 hours.

If we place in one group those requiring manual dilatation and those in whom the breech was broken up at full dilatation, as women apparently in need of extraordinary procedures for successful completion of their labors, the seriousness of these procedures and the appalling fetal mortality they carry with them is brought home to us by the fact that in the 11 times these maneuvers were tried, there were 7 stillborns.

It is an important commentary, I think, that either one or the other of these procedures was considered necessary 6 times out of the total 11, because of poor pains. The significance of this statement will be discussed later. In this group of 11, labor was induced 5 times (3 by bag, 2 with castor oil and quinine), and 3 of these 5 were characterized by poor pains.

These figures show clearly that all three of these procedures lead to an unduly high percentage of bad results, so bad in fact that almost anything would be better. In justification for initiating the procedures, we have our indications, which cannot in all instances be vindicated, I think. Remedy for this sort of thing lies in much stricter indications for their employment and in abandoning the bag as a means of inducing labor except in cases in which the life of the child is not of great consideration.

Other Difficulties in Delivery.—It will be noted that attention has been directed particularly to difficulties arising in the earlier stages of labor rather than to the actual delivery. Most of what is written about breech presentation today concerns the actual delivery, but from a study of these cases, it would seem that it is the course and conduct of the pregnancy and earlier stages of labor which is all important, provided a reasonable technic is employed at delivery. It is true that, in delivering a large baby presenting by the breech, or a normal sized one through a moderately contracted pelvis, skill and a proper technic may determine whether the outcome be a happy one or otherwise; on the other hand, the management of the pregnancy and early labor determines whether a difficult situation shall arise or not. In other words, we should not allow our conduct of a case to precipitate a bad situation from which only extraordinary skill and luck can extract us.

Forceps in Delivery.—Difficulty in extracting the head was mentioned only twice as being the probable explanation of fetal death. It may be that this difficulty will not be encountered when the Piper forceps (or any other type of forceps on the aftercoming head) are employed routinely, but I doubt it. When serious trouble in extraction is met, it is usually because of the unduly large size of the head, or because the head is partially extended high in the birth canal, in neither of which contingencies is the Piper forceps of much use. Forceps are easily applied to the aftercoming head when it is low in the birth canal, and perhaps their application adds finesse to the delivery of the head; the Mauriceau maneuver, carefully performed, is perfectly satisfactory however.

Extension of the arms was mentioned once only as being a contributing cause of fetal death. This would not seem, then, to be a major difficulty. Though sometimes unavoidable, this accident is often due to an error in technic which should be avoided.

Excessive pressure on the head through the abdomen was mentioned once. Though moderate pressure from above is usually necessary to accomplish delivery of the head without excessive pulling from below, it should be applied carefully.

A contracted pelvis appears responsible for difficulty in delivery leading to fetal death in at least two cases. However, we have the following data concerning contracted pelvis. Contracted pelves occurred 15 times in the 285 cases; in one the child was nonviable, and in four cases, stillborn babies were delivered (two at term and two premature). In the two term cases, the generally contracted pelvis was probably a decided factor in causing the fetal deaths (delivery of the aftercoming head by forceps was unsuccessfully attempted), although the cervix may have been a factor. Delivery in the two premature cases was easy and apparently unaffected by the contracted pelvis. The number and variety of pelvic contractions is tabulated below:

Generally contracted typical	8
Simple flat	3
Flat rachitic	2
Generally contracted rachitic	1
Funnel typical	1
	15

This review suggests the lack of wisdom in attempting to deliver a breech in the presence of any but the most minor pelvic contraction except by cesarean section.

Premature rupture of the membranes was known to have occurred ten times (not counting the five times this was done artificially as means of induction). In this group, there were two stillborn babies, both premature. Both died a few days after delivery. In one, there was placentitis, even though the membranes had ruptured only a few hours before the onset of labor; in the other, there was an infected cord, atelectasis, and a small tentorial tear (this labor had been induced by bag). Twice the membranes were ruptured artificially during the course of labor before full dilatation, and stillborn babies were delivered in both instances; the cord prolapsed in one of them. There is no better invitation for the cord to prolapse than to rupture the membranes after labor in breech is well started and before full cervical dilatation.

Prolapse of the cord occurred six times and with two of the babies stillborn. One of the fetal deaths occurred when the cord prolapsed following artificial rupture of the membranes before full cervical dilatation. The other happened in a case in which a bag had been inserted into the vagina inadvisedly.

Recently the policy of inserting a large sized Voorhees bag into the vagina in primiparae has been adopted, with the double purpose of preventing the membranes from rupturing early in labor and of dilating the birth canal, thus making the ensuing breech extraction easy. This procedure was employed six times, once inadvisedly (membranes already ruptured, footling presentation). It worked very well except in this one case in which the cord prolapsed, with resulting stillborn baby. The average length of labor was 18.75 hours.

Birth Injuries.—Others than those found at autopsy as the cause of fetal death, birth injuries were noted six times as follows:

Fractured humerus	2
Fractured femur	1
Fractured clavicle	1
Abrasion in groin	1
Hematoma of thigh	1
	6

None of these injuries occurred in large babies. This seems to be a very small percentage of injuries.

Maternal Mortality and Morbidity.—One woman died from postpartum hemorrhage after a live baby had been delivered by an easy breech extraction. The delivery took place at home several years ago: her condition became bad very rapidly in spite of the usual measures to control hemorrhage, and she died before she could be transported to the hospital. She had had four previous breech deliveries. One patient in the cesarean section group died of disseminated tuberculosis. Her early death was expected, the section being done in order to obtain a live baby from a woman almost at term, hopelessly and acutely ill with tuberculosis, and was in no way attributable to the operation. These two were the only maternal deaths.

Because of varying standards of morbidity, figures are given for the one employed in this clinic (a rise in temperature to 38° C. on one occasion in the puerperium), and also for the standard often employed elsewhere. There were no serious infections in the entire group, and, indeed, the great majority were only technically morbid.

TABLE XI. MORBIDITY

	NUMBER OF CASES	PERCENTAGE OF MORBIDITY
Temperature to 38° twice	43	15.43
Temperature to 38° once	66	23.15

SUMMARY AND CONCLUSIONS

In this series of 285 breech deliveries, the fetal mortality in viable cases was 14.8 per cent, and was evenly divided between multiparae and

primiparae. When the mortality in premature infants, 48.6 per cent, was deducted, the mortality at full term was found to be 9.1 per cent, a figure for which the obstetrician may have been responsible, since there were no technical difficulties in delivering the premature children. The majority of fetal deaths occurred in cases in which there was some type of interference in labor, such as induction of labor, completing the dilatation of the cervix manually or breaking up the breech at full dilatation by traction, and not because of actual difficulty in delivery. An analysis of the various methods of delivery employed, while inconclusive because of the comparatively small number of variations from the usual method of breech extraction followed by the Mauriceau maneuver, did not show one method to be appreciably more advantageous than another. On the other hand, it was the course of the earlier stages of labor which determined the outcome of the delivery; either it was felt that labor must be induced, or there were poor pains and the dilatation of the cervix was manually completed, or for some other reason, a foot was brought down and the breech wedge was broken up when the cervix was in full dilatation; these were the cases which resulted badly. Because of these facts, I feel our conduct of the earlier stages of labor is all important, provided one employs a reasonably good technic at actual delivery. It is granted that labor complicated by poor pains often offers a problem, any solution of which might prove wrong; still, the facts just reviewed are the real problem, and as is shown in this study, indications for interference must be unimpeachable, since such procedures carry a very high fetal mortality. The outcome of our cases should become largely predictable from the characters of the early stages of labor. Indications for cesarean section should be carefully reviewed if there is reason to believe that the labor cannot be terminated without the aid of various means of interference from below.

Maternal mortality was negligible; maternal morbidity, though technically high, was due almost entirely to trivial infection.

One further plea; that the bag be abandoned as a means of inducing or hastening labor, except in cases in which the life of the child is of no consequence.

There are a sufficient number of bad results in this series of cases to demand explanation, and indeed a lesson is forthcoming. On the other hand, the situation is not a gloomy one when it is considered that these cases were not uniformly delivered by residents but more often were handled by a succession of young house officers in training.

The total mortality for recent years, in which two-thirds of the viable cases were delivered, is 9.4 per cent, as compared with 14.8 per cent for the entire series. Furthermore, approximately one-half of the 9.4 per cent mortality occurred in the premature group. So we feel that barring accident and interference, there should be a comparatively small mortality in delivering full term babies presenting by the breech.

RESULTS OF OPERATIONS FOR PROLAPSE OF THE UTERUS AND BLADDER*

GEORGE M. LAWS, M.D., PHILADELPHIA, PA.

(From the Gynecologic Service of the Presbyterian Hospital in Philadelphia)

THIS report is based upon 200 consecutive operations, performed upon 196 patients (Table I) for all degrees of relaxation of the anterior vaginal wall and of prolapse of the uterus.

The results were secured by examination of patients in the hospital Follow-up Clinic and private offices of the operators. Of the 196 patients (Table I), 157 (80 per cent) were followed after operation, the intervals varying from one month to nine years. The percentage of followed patients would have been greater had the study been limited to the years covered by our Follow-up Clinic.

The most important consideration in determining the nature and extent of operative treatment is whether or not the menopause has been passed. As shown in the first table nearly half of the patients had not yet reached the climacteric (Table I).

TABLE I

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
SUMMARY OF FOLLOW-UP

TIME OF OPERATION	TOTAL PATIENTS	NUMBER FOLLOWED
Before Menopause	95	74
After Menopause	101	83
Total	196	157
(Two operations each)	4	4
Total operations	200	
Number followed	161	

OPERATIONS BEFORE THE MENOPAUSE

Plastic Operations Alone.—To avoid possible interference with the childbearing function, we refrained from performing an abdominal sec-

TABLE II

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
BEFORE THE MENOPAUSE
PLASTIC ALONE

Number of Patients		52
Number Followed		44
Results: Good	32	
Improved	6	
Incomplete operation	4	
Failure	2	

*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

tion, when a satisfactory result could be expected from plastic work alone, that is to say, when the uterine prolapse was slight and the bladder lesion was of major importance (Table II). Before operating upon such patients the following points should be considered: (1) the amount of lateral and anteroposterior bladder sag; (2) the presence or absence of a low cystocele; and (3) whether there is loss of bladder control from injured or relaxed vesical sphincter.

In treatment of lateral bladder sag, a plication type of operation is usually sufficient. If marked anteroposterior relaxation exists, the bladder is mobilized and sutured to a higher point on the uterus and, when present, the uterine descent is also corrected. The treatment of low cystocele includes a repair of the overlying muscle and fascia and correction of the uterine descent; the latter is accomplished by reefing the cardinal ligaments in front of the cervix. The perineum is always repaired when cystocele operations are undertaken.

Incontinence due to internal sphincter relaxation is treated by plicating the adjacent tissues with mattress sutures, performing the so-called "Kelly operation." Suburethral, hypertrophic, vaginal folds are resected lest the patient assume that the operation was performed incompletely.

Persistent bladder irritability and incontinence were the chief unsatisfactory results following simple, vaginal plastic procedures. We believe that these two symptoms are due to either the recurrence of a small, low cystocele, which results from failure to have shortened the cardinal ligaments, or to inadequacy of the Kelly operation. The finding of the cervix below its normal position after such operative procedures implies imperfect technic. This low position of the cervix, however, may be symptomless because the firm anterior vaginal wall prevents the forward sliding of the urethra, which is the cause of the urinary symptoms.

It is a common observation that bladder irritability may persist for several weeks after a cystocele operation and eventually disappear. Sometimes, however, preoperative and postoperative urinary symptoms are due to obscure neurogenic or intrinsic urinary tract lesions, and are not necessarily due to error in operative technic. Occult spina bifida is a not infrequent example of a neurogenic lesion causing bladder weakness.

Kelly Operation.—The Kelly operation (Table III) for relaxation of the sphincter was performed upon 20 of the 196 patients. Of the 5 improved patients (Table III) two had 2 Kelly operations each, one of these two having occult spina bifida with some prolapse had had no childbirth injury. The other patient who required two operations had been incontinent since a forceps injury. In all cases in which the Kelly operation was part of the treatment, the results were better when abdominal suspension of the uterus was combined with the plastic work.

TABLE III

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
BEFORE AND AFTER MENOPAUSE
KELLY OPERATION

Number of Patients			20
Number Followed			19
Results:	Good	12	
	Improved	5	
	Failure	2	

Abdominal and Plastic Operations.—For those patients in the childbearing age with advanced degrees of uterine prolapse, or with other indications for intraabdominal surgery, some form of uterine suspension, usually by shortening the round ligaments, has been performed, in addition to a repair of the anterior wall and perineum (Table IV). Some form of cervix operation was carried out upon half of the patients falling in this group. An external Alexander operation was performed upon one patient presenting an inguinal hernia. Of the 35 patients in this entire group, 3 required hysterectomy and 5 were otherwise sterilized.

TABLE IV

OPERATION FOR UTERINE AND BLADDER PROLAPSE
BEFORE THE MENOPAUSE
ABDOMINAL OPERATION AND PLASTIC

Number of Patients			35
Number Followed			24
Results:	Good	20	
	Improved	3	
	Death	1	

The results in this whole group were generally satisfactory. The one death in the 200 operations occurred in this group as a result of thyrotoxicosis in a patient who underwent excision of an adenoma of the thyroid gland simultaneously with the prolapse operation.

Mayo Vaginal Hysterectomy was performed upon 5 patients suffering from procidentia that required removal of the uterus (Table V). Of the followed cases, the unsatisfactory operative result was an ureteral fistula in a patient with irreducible prolapse.

TABLE V

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
BEFORE THE MENOPAUSE
VAGINAL HYSTERECTOMY

Number of Patients			5
Number Followed			3
Results:	Good	2	
	Improved	1	

Abdominal Operations Alone.—Only one patient was treated solely by abdominal operation, shortening of the round ligaments. The result in her case was good.

Interposition Operations.—An interposition operation with sterilization was performed on 2 patients approaching the menopause, with a good result in one case and a failure in the other. In the last mentioned case, good result followed a subsequent abdominal operation, which did not present great technical difficulties.

OPERATIONS AFTER THE MENOPAUSE

After the menopause the majority of patients were treated by various vaginal operations without abdominal section.

Plastic Operations Alone.—Plastic operations alone were done in 39 instances. Of these, the majority were treated by the usual operations on the anterior wall, cervix, and perineum (Table VI).

Vaginal prolapse, following hysterectomy performed elsewhere, was treated by vaginal occlusion with the Le Forte technic in two elderly women. The results were good.

TABLE VI

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
AFTER THE MENOPAUSE
PLASTIC OPERATION ALONE

Number of Patients			39
Number Followed			30
Results:	Good	23	
	Improved	6	
	Failure	1	

Vaginal Enterocele.—Vaginal enterocele was the major lesion presented by 3 women who had been operated upon for prolapse in other hospitals. The slight doubt about the diagnosis in these cases was dispelled by finding fat on incising the posterior vaginal wall. Resection of the hernial sac, and a somewhat unsatisfactory suturing of the uterosacral ligaments gave good results.

Interposition Operations.—The interposition operation has been the treatment of choice for the large cystocele associated with prolapse of a healthy uterus, if the cervix did not extend much beyond the vaginal introitus (Table VII). When limited to patients in this group, the anatomic and functional results have proved satisfactory. The failure noted in Table VII was a case of complete prolapse; however, a good result followed a subsequent abdominal operation. The imperfect results

TABLE VII

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
AFTER THE MENOPAUSE
INTERPOSITION OPERATION

Number of Patients			37
Number Followed			33
Results:	Good	26	
	Improved	6	
	Failure	1	

here, as in other methods of treating vesical prolapse, were persistence of bladder irritability, incontinence, or a small, low cystocele. Routinely the fundus was sutured firmly under the pubic rami, and a perineorrhaphy was always done. Our follow-up emphasizes the necessity for dealing with the sphincter relaxation and the low cystocele without depending wholly upon the interposed uterus.

Vaginal Hysterectomy.—Vaginal hysterectomy was selected for the treatment of advanced prolapse with ulceration (Table VIII).

TABLE VIII

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
AFTER THE MENOPAUSE
VAGINAL HYSTERECTOMY

Number of Patients		8
Number Followed		8
Results: Good	6	
Improved	1	
(Later developed vaginal enterocele)		
No evaluation	1	
(Result masked by fixation of vagina due to progressive cancer)		

It is noteworthy that one patient was a nullipara and had carcinoma of the fundus. (One other patient in the "Operations Before Menopause—Plastic Alone" group, developed carcinoma of the cervix several years after operation.)

Abdominal and Plastic Operations.—Abdominal and plastic operation, with some form of abdominal wall fixation, was the procedure in 13 patients (Table IX).

TABLE IX

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
AFTER THE MENOPAUSE
ABDOMINAL AND PLASTIC OPERATIONS

Number of Patients		13
Number Followed		9
Results: Good	8	
Improved	1	

Abdominal Operations Alone.—Abdominal operation alone consisted of fixing the uterus or cervical stump to the abdominal wall in four patients (Table X).

TABLE X

OPERATIONS FOR UTERINE AND BLADDER PROLAPSE
AFTER THE MENOPAUSE
ABDOMINAL OPERATION ALONE

Number of Patients		4
Number Followed		3
Results: Good	3	

COMMENT

At the beginning of the menopause, it is better in some cases to defer operation until the effect of senile changes can be estimated. The operator can then secure better functional results from plastic work.

In the groups in which any one of several methods of fixation of the uterus to the abdominal wall was a part of the treatment of prolapse, the fixation held firmly in all followed patients. Subsequent elongation of the cervix and other forms of prolapse may follow inadequate repair of the pelvic floor.

Pelvic floor repair has been the important feature of treatment in all groups. The results justify the treatment of the majority of cases of genital prolapse after the menopause by vaginal operations, including subvesical interposition and Mayo vaginal hysterectomy.

It is evident that preoperative diagnosis of all the bladder lesions is essential for successful management.

A study of end-results over a sufficient period of time has constantly directed attention to the importance and difficulty of restoring normal anatomic and physiologic conditions in the bladder base and urethra.

Mayer, A.: Remarks Concerning Thrombosis and Embolism. Monatschr. f. Geburtsh. u. Gynäk. **91:** 39, 1932.

In Mayer's cases of thrombosis and embolism a decided difference was observed between obstetric and gynecologic patients. In recent years there was no increase in the incidence of these complications among the obstetric patients whereas among the gynecologic patients the incidence of thrombosis increased twofold and that of embolism almost trebled. The cause of this increase is unknown unless it is a change in the constitution of the individual as a result of the mental and somatic changes brought about by the war and the hunger blockade. The gynecologic operations which have a predisposition to be followed by thrombosis and embolism are those for myomas, cancer and prolapse of the uterus.

Two important signs of thrombosis are an inexplicable, persistent tachycardia and above all a slight elevation of temperature. Other signs are swelling of the leg and pain in the sole of the foot.

The danger of embolism is less in cases of manifest than in those of latent thrombosis. The probable cause for this is that in outspoken thrombosis the vein is completely blocked and the blood stream is entirely interrupted whereas in unsuspected cases of thrombosis the blood vessel is not completely obstructed so the blood stream can carry away a piece of the thrombus.

There is no effective prophylactic medication. During the operation prophylaxis consists in control of bleeding, perfect asepsis, and protection of the tissues. After operation, exercise and the administration of large amounts of fluid are helpful.

The treatment of pulmonary embolism depends upon whether there is involvement of the heart, the lungs or the brain. In acute cases morphine may help. Surgical cure should be attempted because the death rate from embolism is very high, but usually there is not sufficient warning to permit a timely operation. In many cases death results from subsequent emboli. Furthermore, among 18 fatal cases of embolism, Dietrich found that the embolus was removable in only seven cases.

J. P. GREENHILL.

PATHOLOGY OF THE THYROID GLAND COMPLICATING PREGNANCY*

CHARLES H. FRAZIER, M.D., AND HENRY F. ULRICH, M.D.,
PHILADELPHIA, PA.

(From the Thyroid Clinic, University Hospital)

RESPONSE by the thyroid gland to physiologic demands and to the exigencies of infection have been observed very frequently. While we have no exact knowledge of the modus operandi of the physiologic activity of the thyroid, it seems probable, from observations particularly in regions of endemic goiter, that an insufficient iodine supply will lead to compensatory hypertrophy of the thyroid gland in the course of the ordinary demands of life. Excessive demands, such as pregnancy, may find the gland unable to supply the required amount of thyroxine and hypothyroidism develops. This state, unless severe, may be expected to improve after withdrawal of the added metabolic burden. The goiter so developed will be of the nontoxic diffuse type if the colloid is deposited uniformily or of the nodular type if deposited in a patchy distribution. Recurrent successive stimulations of the former result in a gradual diffuse enlargement, in the latter in coalescence of acini and the formation of adenomas.

In the absence of a deficiency in iodine intake, a perceptible increase in the size of the thyroid gland still can be noted during similar periods of stimulation. Enlargements at puberty, with each menstrual period, and with pregnancy, may be expected. Unlike the gland deficient in iodine, however, the amounts of colloid formed or deposited are not as great, and, these glands return more nearly to their normal size when the stimulation is withdrawn. At times, under these conditions, adenomas may make their beginning but not manifest themselves until later in life.

From the 4000 and upward cases of thyroid disease in the records of the University Hospital, we have selected for the basis of this discussion from a series of 1350 thyroidectomies, 38 patients who developed toxic goiter and 12 who developed simple goiter during pregnancy. The various pathologic conditions of the thyroid gland complicating pregnancy comprise (1) hypothyroidism, (2) simple goiter, (3) toxic goiter, and (4) malignancy of the thyroid.

Hypothyroidism.—It does not follow from what has been said above that only those patients in "iodine poor" regions develop hypothyroidism for hardly a day passes in our thyroid out-patient clinic without our seeing patients from this or neighboring seaboard states with some degree of hypofunctioning thyroid glands. Many women with menstrual disorders, familiar to all of you, so commonly associated with hypothy-

*Presented, by invitation, before the Obstetrical Society of Philadelphia, March 3, 1932.

roidism, are referred to us for metabolic studies by the Gynecological Clinic. The incidence of sterility is high among hypothyroid women, and it is probably a common experience to find these patients pregnant after the hypothyroidism has been relieved by the administration of thyroid extract. One cannot rely wholly on the basal metabolic rate, especially not on a single estimation, in making the diagnosis of hypothyroidism.

Once pregnancy is established in a woman whose thyroid has proved itself to be incapable of regulating normal metabolic processes, the physician must treat that deficiency. Untreated, the pregnancy is apt to be terminated by miscarriage[1] or if carried to term the child may have cretinism or goiter. Litzenberg and Carey[2] have reported women with hypothyroidism who had previously had several miscarriages, carried to term on adequate amounts of thyroid extract. Results from the administration of thyroid preparations should not be looked for too soon after instituting treatment, nor should one, by forcing these therapeutic agents, try to convert quickly the hypothyroid subject into a normal one. It is better to increase the dose slowly and gradually until the desired effect is obtained.

Simple Goiter.—The incidence of simple goiter appearing with pregnancy is variable, and the factors which in our opinion influence the incidence, are locality and the time of appearance of the various reports with relation to the introduction of the use of iodine in the treatment of goiter. The appearance of simple thyroid enlargement during pregnancy has been noted for many years. It is to be expected that in regions where endemic goiter is prevalent that the incidence would be much higher than in this locality. Yoakum[3] and Davis[4] report that in such regions as high as 40 per cent to 60 per cent of pregnant women develop simple goiters. Simple enlargements of the thyroid gland during pregnancy in this locality in the majority of cases quickly subside after delivery. If goiter persists, it rarely impairs the future health of the mother though with successive pregnancies, the goiter may increase in size. Tait[5] first called attention to this phenomena over fifty years ago though since the widespread use of iodine as a prophylaxis against goiter it has not been so frequent. The subsequent enlargement of simple goiter of the colloid type during pregnancy can be prevented by the administration of iodine. In this connection, a word of caution about the indiscriminate use of iodine may be spoken. There is evidence to show that simple, nontoxic, nodular (adenomatous) goiters may be rendered toxic by its use. The number of women requiring thyroidectomy for simple goiter during pregnancy is extremely small. If pressure symptoms threaten the life of the mother, thyroidectomy can be done with safety under local anesthesia. We think it is significant that only 12 of our 1350 women required partial thyroidectomy for a simple goiter which appeared during an earlier pregnancy. No operation was required during the pregnancy in which the goiter appeared, several

months to many years intervening. Eight of the women had had from one to seven pregnancies between the appearance of the goiter and operation, and of these only three were definitely of the opinion that there had been successive enlargements with successive pregnancies. Eleven of the mothers were delivered of normal babies at the end of the pregnancy, during which the goiter appeared; one miscarried as she did again before operation, for a cause undetermined during the period of our observation. She was not hypothyroid. From these observations it can be said that the rôle of simple goiter as a complication of pregnancy is unimportant.

Toxic Goiter.—Thyrotoxicosis in either of its clinical forms, toxic nodular goiter, or toxic diffuse goiter, presents such a variety of symptoms and signs, that frequently it masquerades under the wrong diagnosis and too often is improperly treated. Chief among these erroneous diagnoses are nervous breakdown, heart disease, and some disease of the gastrointestinal tract. Before considering the bearing of thyrotoxicosis upon pregnancy, a word as to the diagnosis. At times the diagnosis is by no means easy or obvious. Nervousness, both subjective and objective, is a frequent accompaniment of the state of pregnancy. Tachycardia is by no means uncommon during pregnancy. Though it is unlikely that obstetricians would mistake the gastrointestinal manifestations of hyperthyroidism for those which frequently accompany pregnancy, the recent contribution by Falls[6] on the use of Lugol's solution in hyperemesis gravidarum is pertinent. He says "certain patients who have died with the clinical picture of hyperemesis gravidarum, have presented a similar picture to that of thyrotoxicosis" and some patients, who had been desperately sick with hyperemesis gravidarum during a given pregnancy were kept free of that complication during successive pregnancies by the administration of Lugol's solution. The incidence of thyroid enlargement during pregnancy has already been mentioned and when present in association with nervous phenomena, tachycardia, and gastrointestinal disturbances, the diagnosis of toxic goiter may be made too quickly. It is well known that during pregnancy, particularly in the latter months, the basal metabolic rate rises. Plass and Yoakum[7] concluded from their observations of 72 women that the basal metabolism during a normal, uncomplicated pregnancy, increased approximately 15 per cent, with a fall to normal in the first few days after delivery. The mechanism of this increase has been explained in the excellent papers by Sandiford and Wheeler[8] and Boothby and Sandiford[9] who presented complete data on respiratory metabolism. They found that the total calories for each hour were 25 per cent greater in the last months of pregnancy than before conception. Their calculations indicated that the increased metabolism was due to the increased protoplasmic mass.

There are various quotations as to the incidence of hyperthyroidism in pregnancy or pregnancy in hyperthyroidism. Yoakum reported

nearly a thousand cases of pregnancy without the association of hyperthyroidism in any. Mussey, Plummer, and Boothby[10] showed the incidence of pregnancy in hyperthyroidism to be 0.6 per cent, and Clute and Daniels[11] at the Lahey Clinic found it to be 0.41 per cent. In our records, we found 44 patients, or 3.2 per cent, in whom thyrotoxicosis began during pregnancy; 21 of these had toxic nodular goiter and 23 toxic diffuse goiter. Of the latter, 7 had thyroidectomy during their pregnancies. The infrequency of associated hyperthyroidism and pregnancy is at once apparent.

Apart from the incidence, we are more concerned with the influence of pregnancy upon hyperthyroidism and the effect of hyperthyroidism upon pregnancy. Clute and Daniels found nothing unusual among their cases of hyperthyroidism in pregnant as compared with nonpregnant women. Multiple stage thyroidectomies were no more frequent in one group than the other. In 68 of 112 cases reported by Seitz[12] the hyperthyroidism was definitely aggravated by pregnancy, 11 had premature labors, 5 miscarried, and 7 died. Following the course of 31 pregnancies in 17 women with hyperthyroidism, Gardiner-Hill[13] felt that the thyrotoxicosis was not made worse by the pregnancies, though in his series there were two stillbirths, eight premature births, and nine miscarriages. Neither did Hyman and Kessel[14] find that pregnancy made the thyrotoxic mothers worse. Nine of their patients had eleven normal children and one stillbirth. Mussey, Plummer, and Boothby agree that thyrotoxicosis is not appreciably influenced by pregnancy. Falls says that if toxic symptoms are present before conception, they are usually aggravated but may be ameliorated by pregnancy. The latter occurred in one case reported by Mussey and Plummer and in one of our patients, though six months later her thyrotoxicosis was reactivated and required a thyroidectomy.

In the collected cases of Gardiner-Hill one-half of the pregnancies terminated either in abortion or premature delivery. In eight of his own cases of primary Graves' disease, developing during pregnancy, there was one full-term stillborn baby and one miscarriage at three months. On the other hand, of the 38 mothers with hyperthyroidism in the series of Mussey and Plummer, 37 were delivered of 36 normal children, including one set of twins and one premature living child. One stillbirth followed forceps delivery.

In our own series, of 38 women who developed toxic goiter during their pregnancies (but who were operated upon by us from several months to several years after delivery), there was but one miscarriage. Eleven of these 38 women had additional pregnancies between the time during which thyrotoxicosis developed, and the date of the thyroidectomy. Four of the mothers had one additional normal pregnancy, two had two, and one had three. Two had one normal pregnancy followed by a miscarriage, one had one miscarriage, and one had three miscarriages.

It is quite improper to draw any statistical conclusions from these quotations since there must be many cases of thyrotoxicosis in pregnant women that are not recorded in the thyroid clinics.

We wish now to present the records of seven patients with toxic diffuse goiters upon whom a thyroidectomy was performed during their pregnancies.

CASE 1.—P. L., aged twenty-two, married, housewife, primipara. Thyrotoxicosis began in 1924. Goiter and exophthalmos appeared in June, 1925. Nervousness, loss of weight, increasing muscular weakness, and marked palpitation were complained of on her first admission to the medical wards of the University of Pennsylvania Hospital in January, 1926. She had taken Lugol's solution for one month prior to admission. Basal metabolic rate was plus 61. She had several series of radium treatments and Lugol's solution intermittently during the next nine months. She was transferred to the surgical service in November, 1926, at which time a right lobectomy was performed. After discharge she became pregnant, in the second month of which she was readmitted to the surgical service for a left lobectomy. Basal rate was plus 70 on this admission. Left lobectomy was performed in February, 1927. Ten weeks later her basal metabolic rate was plus 4. When seen in the eighth month of her pregnancy there was no clinical evidence of toxicity. A normal, healthy baby was delivered at term. She remained so well after delivery that she refused to return for follow-up until ten months after delivery at which time basal rate was plus 8.

CASE 2.—E. W., aged twenty-five, married, housewife, primipara. In November, 1924, she had a series of boiling water injections into the thyroid, then bipolar ligations for toxic diffuse goiter. In May, 1925, subtotal thyroidectomy was performed while the patient was four months pregnant. A normal healthy baby was delivered in November, 1925. She remained perfectly well after delivery until January, 1927, when she developed a recurrence of thyrotoxicosis. She was reoperated upon in July of that year. She was seen at the follow-up clinic four times in the next twenty-one months. At no visit was there any evidence of toxicity.

CASE 3.—H. S., aged twenty-three, married, housewife, primipara. Symptoms of thyrotoxicosis began eighteen months before admission in October, 1927. Exophthalmos had been present for three months. She had taken Lugol's solution for ten months before admission. Basal metabolic rates while in the hospital before operation were plus 66, 62, and 58. She was in the fourth month of her pregnancy. Subtotal thyroidectomy was performed. Basal rates before discharge were plus 33 and 32. Five weeks later basal rate was minus 1, pulse 72. Full term, normal, healthy baby was born in March, 1928. In February, 1929, she reported that she was perfectly well. In March, 1930, her basal rate was plus 7, pulse 72, her exophthalmos was gone, and we considered her entirely well.

CASE 4.—D. H., aged twenty-three, married, housewife, para iii. During her second pregnancy, eighteen months before admission in May, 1929, symptoms of hyperthyroidism had appeared along with thyroid enlargement. Exophthalmos was first noted in January, 1929, following influenza. Basal metabolic rates in the hospital were plus 70, plus 54, and after thirteen days of Lugol's solution, plus 42. After subtotal thyroidectomy and before discharge, her basal rate was plus 30. Seven and a half months after operation she delivered a full-term healthy baby. This pregnancy was the easiest of her three. She felt so well during and after pregnancy that our first follow-up was thirteen months after operation, at which time we first found out that she had been pregnant at the time of thyroidectomy. In May, 1931, her basal rate was plus 16, pulse 72, she had no subjective or objective nervousness, did her usual work without fatigue and felt perfectly well.

CASE 5.—H. M., aged twenty-two, married, factory worker, primipara. First presented herself to our thyroid out-patient clinic in June, 1930, when a diagnosis of toxic diffuse goiter was made. She had had symptoms of toxicity for six months previously. Her basal rate was plus 48. After having been on Lugol's solution for ten days at another hospital, she was admitted to our service July 21, 1930, with a basal rate of plus 16. She was then entering the second month of her pregnancy. Three days after admission a subtotal thyroidectomy was performed. At discharge her basal rate was plus 6. In January, 1931, there was no clinical evidence of toxicity. In February, or the eighth month of her pregnancy, her basal rate was plus 1, pulse 88. Healthy, full-time baby was born March 10. The mother was last seen in November, 1931, when her basal metabolic rate was plus 14 and we considered her perfectly well.

CASE 6.—F. K., aged thirty-four, married, housewife, para iii. Symptoms of thyrotoxicosis began two years before admission following a ruptured ectopic pregnancy. Six months after onset, a goiter appeared. She was admitted to the hospital May 18, 1931, with a basal metabolic rate of plus 38. She had a definitely hyperplastic gland, exophthalmos, hyperidrosis, and tachycardia and tremors. Her last period had been on December 9, 1930. A chronic, bronchial asthma had become much worse since her pregnancy began. Subtotal thyroidectomy was performed on May 27, 1931. At discharge her basal rate was plus 2. Her pregnancy continued uninterrupted to full term, her baby being born September 16, 1931. She returned for follow-up this February, when her basal rate was plus 3, and she showed no evidence of toxicity.

CASE 7.—E. F., aged thirty-three, married, housewife, para iii. Her last regular period was January 14, 1931. Her pregnancy was uneventful until late in April when she developed symptoms and signs of toxic diffuse goiter. On May 16, 1931, she was admitted to the hospital. Lugol's solution, minims 30 daily, started at once, adequate sedatives and rest in bed, except for bathroom privileges, was the program. Her pulse rate was 160. After being on Lugol's solution for one week her basal metabolic rate was plus 40. Five days later it dropped to plus 24. On June 2, 1931, a subtotal thyroidectomy was performed. Her convalescence was uneventful as was the remainder of her pregnancy which ended at full term in the delivery of a normal baby. When seen March 2, 1932, her pulse was 88, and she had no clinical evidence of thyrotoxicosis. Her basal rate was plus 24, but she had a cold and had driven her car 30 miles (after a four hour sleep the night before) to come for the test. She feels perfectly well.

This is an impressive and convincing demonstration and forces us to the conclusion that patients with toxic goiter complicating pregnancy tolerate thyroidectomy as well as those not pregnant. All of the children of these mothers were normal and healthy.

Recurrences or relapses after thyroidectomy does occur in a small percentage of cases, but in none of 28 of such cases in our clinic was recurrence caused by pregnancy. We occasionally have the opportunity in the two-year follow-up period after thyroidectomy of observing the course of pregnancy. A brief synopsis of three such cases follows:

CASE 8.—M. H., aged twenty-eight, developed thyrotoxicosis during her first pregnancy which terminated normally in December, 1928. All symptoms were aggravated during lactation. Despite iodine therapy and maximum rest, she came to us for thyroidectomy in April, 1930. Basal metabolic rate was plus 34. Subtotal thyroidectomy was performed May 3, 1930. Basal rate on May 14 was plus 6. In October, 1930, she returned for follow-up being four months pregnant. Her basal

metabolic rate was minus 11, pulse 72, and blood pressure 102/56. On March 26, 1931, a normal, full-term living child was born. She reported that her pregnancy had been entirely uneventful. We last saw her in May, 1931, when we agreed with her that she was perfectly well. Her basal metabolic rate was minus 6, pulse 76.

CASE 9.—W. W., aged twenty-five, had had a right lobectomy and left superior polar ligation for toxic diffuse goiter at another hospital four years before coming to us. She was frankly toxic on admission to our service on May 1, 1930. Basal rate was plus 54, pulse 140. After preparation with iodine, a left lobectomy was performed on May 8. Basal rate on the sixth day postoperative was plus 20. In September, 1930, her pulse was 80 and basal rate plus 15. There was no clinical evidence of toxicity. In May, 1931 she was in the seventh month of her pregnancy. Basal metabolic rate was plus 32, pulse 84. The clinical evidence did not substantiate the basal rate. In September, 1931, when last seen, she reported that her pregnancy had proceeded uneventfully to term when a normal, healthy baby was born in July. In September, 1931, her basal rate was plus 3 and pulse 84.

CASE 10.—C. C., aged thirty-eight, had subtotal thyroidectomy for toxic diffuse goiter in October, 1930. In May, 1931, basal metabolic rate was plus 5, pulse 82. She was then two months pregnant. In September, 1931, blood pressure was 140/70, pulse 90, basal metabolic rate plus 19. We considered her mildly thyrotoxic and started Lugol's solution, minims 3 daily. She was last seen February 3, 1932, nearing the eighth month of her pregnancy. Blood pressure 125/70, pulse 96, basal rate plus 21. She had no tremors; there was no demonstrable evidence of toxicity, and she denied any subjective nervousness. She was instructed to continue on iodine until after delivery.

It appears from our experience and that of others, that pregnancy is not a factor in the production of recurrent thyrotoxicosis. In the series of Clute and Daniels 53 women who had had thyroidectomy for thyrotoxicosis bore 69 children subsequent to operation, with only one developing what might have been recurrent toxicity. If evidence of toxicity does develop during pregnancy, the judicious use of iodine probably will carry the mothers safely to term, when the symptoms will subside by virtue of their being relieved of the added metabolic burden.

Having reviewed in our experience and the experiences of others the incidence of toxic goiter complicating pregnancy and the effect of toxic goiter upon the outcome of pregnancy, the question of importance alike to obstetrician and surgeon is this: under what circumstances should surgical treatment be considered appropriate, or, if you choose, imperative when thyrotoxicosis complicates pregnancy? Perhaps we should preface our answer to this question by a statement as to the termination of pregnancy. Are there any circumstances under which pregnancy should be terminated because of thyrotoxicosis? In several of our cases this had been seriously considered before we had been called in consultation. There may be aggravated forms of toxicity, in which such a course might seem desirable; if so, we have not seen them. And we would like to record our opinion in emphatic terms that the termination of pregnancy should be discountenanced. Let us remind you that in our series of thyroidectomies in pregnant women there were no fatalities and the mothers were delivered of normal babies.

As for the indications for the surgical treatment of toxic goiter in

pregnancy, one should be influenced wholly by the degree of toxicity. In toxicity of mild degree, we advocate a trial course of iodine. If the toxic symptoms subside altogether, or are kept under reasonable control, the question of operation may be deferred until after delivery. But, be it remembered that patients whose toxicity during the early months of pregnancy has been controlled by iodine, may become iodine fast and get out of control toward the end of pregnancy. Thyroid crises occasionally develop with alarming rapidity even while the patients are being properly treated. If the toxicity is not favorably influenced by iodine, if the toxic state persists or becomes aggravated, a thyroidectomy offers the best prognosis for both mother and child. We have had no cases of abortion. In pregnancies that follow thyroidectomy, the obstetrician should be on the look-out for the slighest suggestion of a relapse and at once institute iodine therapy.

As to the time at which the operation should be performed, that is, whether in the early or late months of pregnancy, one should not be influenced by the pregnant state but by the degree of toxicity. As a matter of fact, in our decisions for or against operation, we have, except in the milder forms of toxicity, disregarded the pregnant state altogether and considered the patient only as a subject of thyrotoxicosis. The likelihood of the degree of toxicity becoming more advanced as the pregnancy advances, has prompted us to advise operation once the diagnosis is established.

Malignancy of the Thyroid.—Carcinoma and sarcoma of the thyroid gland are not uncommon. Two per cent of all the nodular goiters removed at the University Hospital have been malignant. The early diagnosis of malignancy of the thyroid is difficult and too often it goes unrecognized until it is too late to cure the patient. Our experience with carcinoma of the thyroid occurring in a pregnant woman is limited to the case summarized here.

CASE 11.—M. P., aged thirty, married, white woman, para ii. During her first pregnancy in 1929, she developed a unilateral nodular enlargement of the thyroid gland. Her pregnancy terminated normally with the birth of a healthy, normal child. The thyroid enlargement gradually disappeared after delivery. In March, 1931, when the patient was entering the second month of her second pregnancy, the goiter reappeared. Until June the tumor was slow growing. From then on its growth was rapid and soon produced a severe hacking cough with dyspnea on exertion. Because of these complaints, the patient was admitted to the Medical Service of the University Hospital, July 22. On admission she was orthopneic, slightly cyanosed about the face and neck, had "crowing" respirations, and was in great distress. There was a large visible mass in the lower part of her neck. She was then entering the sixth month of her pregnancy.

Roentgenogram of her neck and chest showed an enormous thyroid encroaching upon the lumen of the trachea with a large, substernal mass. Bronchoscopic examination revealed displacement and compression stenosis of the trachea, also a small fungating mass of tissue in the trachea.

The patient was transferred to our service on July 30, 1931. The following day we operated upon her. A huge tumor mass was found filling the neck. Neither the

lateral nor the inferior limits of the tumor could be determined. A piece of the tumor the size of an orange, was removed from over the trachea. The thyroid isthmus was resected. These procedures bared the trachea for a distance of 2 cm.

The patient convalesced satisfactorily and was discharged August 10 after receiving the first of a series of x-ray treatments over the tumor. She received x-ray treatments again on August 12 and August 14. On August 16, because of urgent dyspnea she was admitted to the Bronchoscopic Service where tracheotomy was performed. Again after discharge intensive x-ray treatments were continued.

Despite these events, her pregnancy continued to term. On November 30, 1931, a normal living child was delivered. The mother was still under treatment by the X-ray Department. When last seen she was quite comfortable with the tracheotomy tube still in place. The tumor mass in her neck was considerably smaller than it was on her discharge from the hospital.

The treatment of malignancy of the thyroid must be radical. When the neoplasm appears to be confined to one lobe, complete lobectomy and excision of adjacent lymph nodes, infiltrated fascia and muscles should be followed by x-ray therapy. When complete excision cannot be done, relief from or prevention of tracheal compression should be the aim of whatever operation is attempted. Baring the trachea greatly facilitates tracheotomy should such become necessary. The presence of the state of pregnancy, associated with malignancy of the thyroid gland, does not alter our program of partial or complete excision of the tumor followed by x-ray therapy.

SUMMARY AND CONCLUSIONS

1. An appreciable response by the thyroid gland to the state of pregnancy is frequently noted.

2. Hypothyroidism in a pregnant woman may cause miscarriage; or if a living baby is delivered, the baby may have cretinism or a goiter. The judicious administration of thyroid extract to pregnant, hypothyroid mothers will prevent these complications.

3. The development of simple goiter during pregnancy usually does not interfere with the normal course of events and does not affect the child. The use of iodine during pregnancy may prevent the development of simple goiter.

4. Nodular goiters, which by their size or location, threaten the life of the mother by pressure on the trachea and recurrent laryngeal nerves, should be removed regardless of pregnancy.

5. Thyrotoxicosis developed during pregnancy in 3.2 per cent of the women upon whom thyroidectomy has been performed in our clinic.

6. The records of seven patients with toxic goiter, upon whom thyroidectomy was performed during their pregnancies, are reported. All of the pregnancies went to term and the mothers were delivered of normal babies.

7. Pregnancy should not be voluntarily terminated because of the development of thyrotoxicosis.

8. Mild degrees of thyrotoxicosis during pregnancy may be controlled by the use of iodine.

9. In cases where severe degrees of thyrotoxicosis complicate pregnancy or in milder degrees of toxicity not controlled by iodine, thyroidectomy should be performed at once.

10. The recurrence of thyrotoxicosis during pregnancy, subsequent to thyroidectomy for toxic goiter, may be prevented by the administration of iodine.

11. The treatment of malignant tumors of the thyroid should be carried out without regard for an associated pregnancy.

REFERENCES

(1) *Mussey, R. D., and Plummer, W. A.:* J. A. M. A. **97**: 602, 1931. (2) *Litzenberg, J. C., and Carey, J. B.:* Am. J. Obst. & Gynec. **17**: 550, 1929. (3) *Yoakum, W. A.:* Am. J. Obst. & Gynec. **15**: 617, 1928. (4) *Davis, C. H.:* J. A. M. A. **87**: 1004, 1926. (5) *Tait, A.:* Quoted by Gardiner-Hill. (6) *Falls, F. H.:* Am. J. Obst. & Gynec. **22**: 882, 1931. (7) *Plass, A., and Yoakum, W. A.:* J. Am. Gynec. Soc. **54**: 164, 1930. (8) *Sandiford, I., and Wheeler, T.:* J. Biol. Chem. **62**: 329, 1924. (9) *Boothby, W. M., and Sandiford, I.:* Am. J. Physiol. **96**: 191, 1931. (10) *Mussey, R. D., Plummer, W. A., and Boothby, W. M.:* J. A. M. A. **87**: 1009, 1926. (11) *Clute, H. M., and Daniels, D. H.:* Am. J. M. Sc. **179**: 477, 1930. (12) *Seitz, L.:* Trans. Deut. Ges. f. Gynäk. **1**: 213, 1913. (13) *Gardiner-Hill, H.:* Lancet **216**: 210, 1929. (14) *Hyman, H. T., and Kessel, L. J.:* J. A. M. A. **88**: 2032, 1927.

3400 Spruce Street. *(For discussion, see page 941.)*

UNCOMPLICATED PROLAPSE OF THE OVARY, DUE TO ELONGATION OF THE INFUNDIBULOPELVIC LIGAMENT, AND ITS TREATMENT*

Barton Cooke Hirst, M.D., and I. Andrussier, M.D.,
Philadelphia, Pa.

THERE are some conditions in gynecology, probably in other branches of medicine as well, that are apparently ignored or forgotten periodically, although known for a considerable time. This is true of uncomplicated prolapse of the ovary, unassociated with displacement of the uterus, pelvic inflammation or other pelvic pathology.

It was discussed by Rigby as long ago as 1850, by the members of the Boston Gynecological Society in 1872; was noticed by Skene in 1878, by Paul Mundé in 1879. Imlach in 1886 advocated the suture of the hilum of the ovary to the relaxed infundibulopelvic ligament near the brim of the pelvis and called it oöphororrhaphy. Saenger's notable article on the subject in 1896, like so much that Saenger did, established the condition on a scientific basis as to its etiology and proposed for the first time a logical treatment. The following year prolapse of the ovary, with a suggestion for its treatment, formed part of a contribution to the transactions of the Gynecological Section of our College of Physicians. Of the four cases reported at that time one of the patients had been operated upon two years before by a procedure very much like that of Saenger's but independently as the operation had been done a year before the appearance of his paper. The latter had in his first operation passed a stitch through the ovarian fimbria and the same thread through a fold of the peritoneum over the infundibulopelvic ligament, tying the two ends of the thread together, thus shortening the ligament. The contributor to the Gyneco-

*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

logical transactions had caught the infundibulopelvic ligament just at the outer edge of the ovary and had then passed the stitch through a fold of peritoneum and pelvic fascia in front of the iliac vessels, thus practically obliterating the suspensory ligament of the ovary, a procedure since modified and improved.

In 1903 Mauclaire proposed an operation for prolapse of the ovary by buttonholing the broad ligament below the round ligament, passing the ovary through the opening after cutting the ovarian fimbria and fastening it on the anterior face of the broad ligament by two stitches, one at each end of the ovary. Then if the patient desired children the fimbriated extremity of the tube was fastened in immediate proximity to the ovary.

Barrows, in the *Medical Record* of October, 1904, proposes the same procedure except that he passes the ovary through the broad ligament above instead of below the round ligament. Barrows did his first operation in 1901, two years before Mauclaire published the account of his. In 1907, George Gray Ward advocating Barrow's procedure, gives an extensive and interesting review of the subject. In the course of this review he expresses surprise that there are specialists who entirely ignore the condition and quotes one man of reputation who confesses entire ignorance of the subject. Ward might have been still more astonished at Stoeckel's recent statement (1928) that the whole thing was nonsense; ("Die Ovariopexie ist ein Unsinn") a rather summary dismissal of a matter that has interested many men of large experience, more than average powers of observation and good judgment.

In 1909 Stratz published an interesting paper on all the displacements of the ovary, reporting five cases of forward displacement and quoting Sellheim's 44 cases of upward displacement (imperfect descensus). Stratz's proposition for the correction of too wide an excursion of the ovary from its normal position is to fasten both ends of it to the round ligament, a proposition, to judge from one of his pictures, based on the mistaken supposition, we believe, that the displacement of the ovary is due to abnormal elongation of the ovarian ligament.

Reiffersheid in 1924 dismisses the treatment of prolapsed ovary with the statement that Saenger's ovariopexie must very rarely be required. Kelly in 1928 acknowledges the importance of the condition and gives a good description of the symptoms, but proposes plicating the uterosacral ligaments to reform a fossa ovarica in which the ovary may rest and advocates shortening the tuboovarian ligament. Neither of these procedures, in our judgment, would correct a descensus ovarii. Von Jaschke in 1929 states that only very rarely would the Saenger operation be indicated. And finally the book on *Gynäkologische Operationslehre by Peham and Amereich*, published in 1930 says nothing about it.

The occurrence of simple, uncomplicated prolapse of the ovary is rare, is not always provocative of troublesome symptoms and moreover it may occur and recur at varying intervals, the ovary meanwhile occupying a normal position. We have had an opportunity to observe this phenomenon in several instances. For example in a multipara, in consequence of manual reposition, tampons, knee chest posture and the temporary use of a pessary, the ovary would remain in good position for a time. Then, suddenly, the ovary would prolapse to the bottom of Douglas' pouch. The patient was immediately aware of what had happened; became nauseated, incapacitated and had to be sent home in a cab. In another patient, a young nullipara under observation for a couple of years, the ovary, at first totally prolapsed, had remained in good position after manual reposition for nine months when, on alight-

ing from a street car, the prolapse suddenly recurred with its distinctive symptoms. Both these patients were permanently relieved by the operation described as the first procedure presented to the Gynecological Section of the College.

In addition to this peculiarity in its symptomatology of sudden occurrence and recurrence, with nausea and disability, there is often, as might be expected, extreme pain on defecation and dyspareunia.

Of late years the operation first described by us has been modified and simplified. It now consists simply of three insertions of the threaded needle directly under the infundibulopelvic ligament: one next to the ovary, one in the middle of the ligament and one at its pelvic extremity, avoiding the blood vessels. By tying the ends of the suture together the whole length of the ligament disappears, or by making the last insertion of the needle a little short of the pelvic end of the ligament a sufficient reduction of its length is secured to bring the ovary to a normal level.

It appears from this technic that we accept Saenger's explanation for prolapse of the ovary: That it can be due only to an abnormal length of its suspensory ligament. In addition to its employment for ovarian prolapse per se, we find this operative procedure of use when operating for retrodisplacement of the uterus or after salpingectomy for pelvic infection. For if an elongated infundibulopelvic ligament is overlooked and one may be three times or more the length of its fellow, or both may be abnormally lengthened, then the patient, relieved of her major pelvic pathology, may subsequently suffer from the disagreeable symptoms of ovarian prolapse.

REFERENCES

(1) *Sänger, M.:* Zentralbl. f. Gynäk. **20**: 241, 1896. (2) *Hirst, B. C.:* Trans. Section Gynec. Coll. Phys. Phila. **3**: 19, 1897; and Am. J. Obst. **35**: 536, 1897. (3) *Mauclaire:* La Semaine Gynécologique, pp. 273 and 281, 1903. (4) *Barrows, Charles C.:* Med. Rec. **66**: 601, 1904. (5) *Ward, George G.:* J. A. M. A. **49**: 1507, 1907. (6) *Stratz, C. H.:* Ztschr. f. Geburtsh. u. Gynäk. **65**: 283, 1909. (7) *Reifferscheid, Karl:* Die Lageveränderungen der Adnexe. *Halban-Seitz:* Biologie und Pathologie des Weibes, **3**: 682-683, 1924. (8) *Stoeckel, Walter:* Lehrb. d. Gynäk. 508, 1928. (9) *Kelly, Howard A.:* Suspension of Prolapsed Ovary, H. A. Kelly and Collaborators: Gynecology, p. 486, 1928. (10) *von Jaschke, Rudolph Th.:* In Veit-Stoeckel's Handb. d. Gynäk. **5**: Part 1, 929, 1929. (11) *Peham, H., and Amreich, J.:* Gynäkologische Operationslehre, 1930.

(For discussion, see page 942.)

REVIEW OF 570 FORCEPS OPERATIONS*

M. Alexander Novey, M.D., Baltimore, Md.

(From the Department of Obstetrics, University of Maryland)

DeLEE states that "the forceps of obstetrics is an instrument designed to extract the fetus by the head from the maternal passages, without injury to it or to the mother. As soon as the right of either is encroached upon, the instrument ceases to be the forceps of obstetrics but becomes simply an instrument of extraction, similar to the craniotomy forceps and not so good."

The incidence of instrumental delivery in recent years has grown so enormously that a glimpse at the White House Conference Questionnaire concerning deliveries during 1929 might not be out of place. Two hundred and seven general hospitals reported 120,999 deliveries with 21,097 forceps, or 17.4 per cent; 16 obstetric clinics reported 24,813 deliveries with 5,075 forceps, or 20.4 per cent. Taken together there were 145,812 deliveries with 26,172 forceps, or 17.9 per cent, an incidence of one forceps operation in every 5 or 6 deliveries. If forceps were applied where actually needed, a figure of not over 5 per cent should represent the incidence of its use.

The group of cases which it is my privilege to present consists of 570 forceps deliveries occurring in a series of 16,442 cases, covering a period of approximately ten years, delivered on the University of Maryland indoor and outdoor services and the Health Department Obstetrical Service.

Number of deliveries 16,442
Number of forceps ..... 570 (1 in 29)
High 63, Mid 229, Low 278.

INDICATIONS

High Forceps:			
Contracted pelvis	22	Face presentation	3
Posterior occiput	13	Aftercoming head	2
Transverse arrest	7	Prolonged labor	2
Fetal distress	5	Placenta previa	1
Prolapsed cord	4	Antepartum eclampsia	1
Maternal distress	2	Not stated	1
Mid Forceps:			
Posterior occiput	70	Abruptio placentae	5
Prolonged labor	48	Maternal heart disease	5
Fetal distress	35	Maternal tuberculosis	1
Contracted pelvis	26	Aftercoming head	1
Transverse arrest	14	Face presentation	1
Maternal distress	9	Prolapsed cord	1
Eclampsia	8	Not stated	5
Low Forceps:			
Prophylactic	141	Transverse arrest	5
Prolonged labor	46	Maternal distress	2
Fetal distress	30	Face presentation	2
Posterior occiput	25	Pneumonia	2
Eclampsia	12	Abruptio placentae	1
Prolapsed cord	6	Placenta previa	1
Maternal heart disease	5		

*Read before the Obstetrical and Gynecological Section of the Baltimore City Medical Society, January 15, 1932.

SUMMARY OF INDICATIONS

Prophylactic	141	Maternal heart disease	10
Posterior occiput	108	Face presentation	6
Prolonged labor	96	Abruptio placentae	6
Fetal distress	70	Aftercoming head	3
Contracted pelvis	48	Placenta previa	2
Transverse arrest	26	Maternal tuberculosis	1
Eclampsia	21	Pneumonia	2
Maternal distress	13	Not stated	6
Prolapsed cord	11		

TABLE I. MATERNAL MORTALITY AND MORBIDITY

High Forceps:			
Mortality		0	0.0 per cent
Morbidity		15	23.8 per cent
Sufficiently severe to require more than two weeks in hospital 5, 7.93 per cent			
Mid Forceps:			
Mortality		3	1.31 per cent
Eclampsia	1		
Eclampsia with pneumonia	1		
Puerperal infection	1		
Morbidity		54	23.58 per cent
Sufficiently severe to require more than two weeks in hospital 11, 4.80 per cent			
Low Forceps:			
Mortality		7	2.51 per cent
Cardiac (on table)	2		
Acute toxemia	1		
Acute yellow atrophy	1		
Eclampsia	3		
Morbidity		54	19.40 per cent
Sufficiently severe to require more than two weeks in hospital 21, 7.55 per cent			
Total maternal mortality		10	1.76 per cent
Total maternal morbidity		123	21.57 per cent
Sufficiently severe to require more than two weeks in hospital		37	6.66 per cent

The following is a brief résumé of the fatal cases:

MID FORCEPS

Case 1.—Colored primipara aged fifteen years, a service case. Physical examination negative and pelvic measurements normal. This patient had a prolonged first and second stage of labor. The fetus presented as an occipitoposterior. A double application of forceps was done and a stillborn child delivered. Following delivery the mother developed a very severe postpartum infection and died.

Case 2.—Colored primipara aged twenty years, a service case, with a diagnosis of antepartum eclampsia. The pelvis was generally contracted with an external conjugate of 18 cm. An occipitoposterior presentation was diagnosed and the patient was delivered by a mid forceps operation. Following delivery the patient continued to have convulsions and in a short time developed pneumonia and after remaining in the hospital for twenty-nine days, she died.

Case 3.—Colored para iii aged twenty-eight years, a service case, with a diagnosis of antepartum eclampsia. The patient had previously delivered twice normally. Her pelvic measurements were normal. The patient went into labor and her convulsions continued. A mid forceps operation was performed and a stillborn infant weighing 8 pounds was delivered. This child was the first of twins. The second baby was delivered as a breech presentation. The patient died thirty hours after admission to the hospital, her temperature going as high as 110° F.

LOW FORCEPS

Case 4.—White primipara, twenty-two years, service case. Physical examination was unsatisfactory because the patient was comatose on admission. Delivered by low forceps of a child weighing 1450 gm. Shortly after delivery the patient died, and at autopsy a diagnosis of acute yellow atrophy of the liver was made.

Case 5.—Colored para ii, aged twenty-eight years, a service case. The patient had been delivered previously by means of forceps of a living child. Her pelvic measurements revealed a generally contracted pelvis with an external conjugate of 18 cm. A stillborn child was delivered with low forceps, the head presenting as an R. O. P. While the patient was being delivered she suddenly ceased to breathe, death being due either to a cardiac condition or to the anesthetic.

Case 6.—White primipara aged twenty, a private case with a history of having had twelve antepartum convulsions. The patient was treated conservatively and allowed to go into labor. When the labor was almost terminated a low forceps operation was performed and a stillborn child delivered. The eclamptic attacks continued until the patient died. No anesthetic was used.

Case 7.—Colored primipara aged twenty-three, a service case, with a history of having had four antepartum convulsions. The patient was in deep coma on admission, and it could be seen that she would cease to breathe very shortly. A thirty-six weeks' macerated fetus was delivered with low forceps without an anesthetic, and the patient died while being delivered.

Case 8.—Colored para vi, aged thirty-two, a service case. Her pelvic measurements were normal. The patients was admitted in extremis with a temperature of 103° F., a pulse of 160 per minute and respirations 52 per minute. Fetal heart not heard on admission. Her first and second stages of labor had been prolonged, the patient was delivered without an anesthetic with low forceps of a stillborn child weighing 8½ pounds. A diagnosis of obscure acute toxemia was made. Autopsy was not obtainable. The patient died shortly after admission.

Case 9.—White primipara, aged nineteen, a service case, with a history of having had several antepartum eclamptic attacks. External conjugate 18 cm. The patient was treated conservatively, and when the head reached the perineal floor, a low forceps operation was performed and a stillborn child weighing 4 pounds 14 ounces was delivered. The eclampsia continued and the patient died in spite of treatment.

Case 10.—Colored para x, aged thirty-eight, a service case. Her pelvic measurements were normal and she had previously been delivered normally 5 times and by forceps 4 times, a living child having been obtained in each instance. This case was very similar to Case 5. An easy low forceps operation was performed and a child weighing 9 pounds 13 ounces was delivered through a very relaxed outlet. While the patient was being delivered, she ceased to breathe, and death was probably due to either a cardiac condition or to the anesthetic.

The mortality and morbidity figures given above represent the total uncorrected results. The morbidity figures reported are based upon temperatures taken every four hours and any elevation above 100.4° F. for two successive days placed the patient in the febrile group. It can be seen that the majority of the patients in this group were discharged from the hospital within two weeks after delivery, a special classification having been made for those patients requiring more than two weeks' hospitalization. Any attempts at giving corrected mortality and morbidity figures are always filled with danger. For example, of the three mothers who died in the mid forceps group, the two cases of eclampsia might very

well be omitted from so-called forceps deaths, leaving only the death from puerperal infection attributable to this operation. This would give us a corrected maternal mortality for mid forceps of 0.40 per cent. Considering the low forceps groups in the same manner, the cases of acute toxemia, acute yellow atrophy and eclampsia not being directly attributable to the forceps operation, there remain only the two patients who died on the table, either from a cardiac condition or as anesthetic deaths. This would give us a corrected mortality for low forceps of only 0.70 per cent.

If we were to consider the case of the patient who died of puerperal infection following a mid forceps operation as the only death attributable to the operation itself, the corrected maternal mortality would be 0.176 per cent, and if we were to include the two patients who died on the delivery table of either a cardiac condition or because of the anesthetic, the corrected maternal mortality would be 0.53 per cent.

TABLE II. RESULTS TO CHILD

		STILLBORN		DYING IN TWO WEEKS	
High forceps: (63)		22, 34.9 %		6, 9.52%	
Intracranial hemorrhage	7		Intracranial hemorrhage	5	
Intrauterine asphyxia	5		Hemophilia	1	
Maternal toxemia	3				
Prolapsed cord	3				
Abruptio placentae	2				
Placenta previa	1				
Macerated	1				
Mid Forceps: (229)		28, 12.22%		18, 7.86%	
Intrauterine asphyxia	16		Intracranial hemorrhage	11	
Intracranial hemorrhage	4		Prematurity	5	
Maternal toxemia	3		Intrauterine asphyxia	1	
Macerated	3		Congenital atelectasis	1	
Prolapsed cord	1				
Abruptio placentae	1				
Low Forceps: (278)		21, 7.55%		6, 2.15%	
Maternal toxemia	8		Prematurity	2	
Intrauterine asphyxia	4		Maternal toxemia	2	
Prolapsed cord	4		Intracranial hemorrhage	1	
Macerated	4		Congenital atelectasis	1	
Abruptio placentae	1				

Total Results to Child

Stillborn	71	12.45%
Dying in two weeks	30	5.26%
Total Infant Mortality	101	17.71%

A careful study of the infant mortality reveals a number of causes of death for both stillbirths and infants dying in the first two weeks of life, which are not attributable to the forceps operation. Among the causes of stillbirth in the high forceps group only the 7 cases of intracranial hemorrhage and the 5 cases of intrauterine asphyxia should be attributed to the operation, giving us a corrected stillbirth mortality figure for high forceps of 19.04 per cent. Of the children dying in the first two weeks

in the high forceps group the one case of hemorrhagic disease of the newborn cannot be attributed to the operation itself and the corrected figure in this instance is 7.93 per cent.

Similarly, in the mid forceps group only the 16 cases of intrauterine asphyxia and 4 instances of intracranial hemorrhage are assignable to the mid forceps operation, giving us a corrected stillbirth mortality figure of 8.7 per cent. Of the infants dying within the first two weeks in this group, the 5 infants dying of prematurity and one of congenital atelectasis may be eliminated as being caused by the forceps operation with a corrected mortality figure of 5.2 per cent.

Similarly, in the low forceps group one may consider only the 4 cases of intrauterine asphyxia and the one case of intracranial hemorrhage as being attributable to the operation, giving a stillbirth mortality figure for this group of 1.43 per cent and for those children dying within the first two weeks of life a corrected figure of 0.359 per cent.

Summarizing this attempt to arrive at a figure representing a corrected infant mortality, we find that the stillbirth rate for high, mid, and low forceps combined is 5.96 per cent. The rate for infants dying within the first two weeks of life for the three groups is 3.15 per cent. These figures compare with the uncorrected mortality figures of 12.45 per cent and 5.26 per cent respectively. The total corrected infant mortality including both stillborn infants and those dying within the first two weeks of life is 9.4 per cent, as compared to 17.71 per cent, the total uncorrected infant mortality is given in Table II.

TABLE III. MISCELLANEOUS

Private	204	36.40%
Service	362	63.96%
White	341	60.24%
Black	225	39.75%
Primipara	419	74.02%
Multipara	147	25.97%
16 years or less	61	10.77%
17 to 25 years	306	54.06%
26 to 35 years	164	28.97%
36 to 50 years	35	6.18%

EPISIOTOMY		FIRST DEGREE TEAR		SECOND DEGREE TEAR		THIRD DEGREE TEAR	
263	46.46%	61	10.77%	152	26.85%	9	1.59%

(Six of these were occipitoposterior)

CONTRACTED PELVIS (48)		INFANT MORTALITY	
High forceps	7	5	71.42%
Mid forceps	27	9	33.33%
Low forceps	14	3	21.42%

The entire series of cases were classified according to pelvic measurements, and there were found 48 cases of contracted pelves with external conjugates of 18 cm. or less. It is only fair to state that practically all

of these occurred before the day of the popularity of laparotrachelotomy which has only been in the past few years and today very few of these cases would be subjected to delivery with forceps. The figures on this group of cases are most interesting. There were 7 patients delivered by high forceps with an infant mortality of 71.42 per cent; 27 patients of mid forceps with a mortality of 33.33 per cent; and 14 patients of low forceps with a mortality of 21.42 per cent. The latter group were delivered after a prolonged labor had done its damage to the fetus. It is quite likely that practically all of these 48 cases would be eliminated from this report if the deliveries occurred today rather than a number of years previously.

I have just a word to add in conclusion. From the figures which I have presented, one can, with assurance, draw the conclusion that at best the obstetric forceps is a dangerous instrument which should be used only upon suitable indications and then only by one skilled in its application. There is no place in obstetrics for the so-called "convenience" forceps. Figures on both the immediate and late injuries to the child show beyond a doubt that the higher the station of the fetal head at the time of delivery, the more damage is done. From 1919 to 1929 1,147 forceps deliveries occurred at the Bonn Woman's Clinic according to H. Krukenberg. The percentage of incidence was 6.2 per cent. Of the live children 72.7 were traced. Fifty-four high forceps revealed 1.9 per cent late injuries; 144 mid forceps revealed 1.4 per cent late injuries; and 739 low forceps revealed 0.13 per cent late injuries. I apologize for quoting so many statistics but the group of cases traced by Krukenberg is so far superior to any other that I have found in the literature, that I feel the figures are worth mentioning.

F. C. Irving reports 13,849 babies born at the Boston Lying-In Hospital from 1920 to 1929.

Clinically, 99 cases of intracranial hemorrhage were diagnosed or one in every 140 births. From 1909 to 1929, 182 autopsies were performed in which the head was examined. Of these 73 or 40 per cent showed intracranial hemorrhage as the cause of death.

Holland, Spencer, Schott, Archibald, Warwick, Crothers, and others state that intracranial hemorrhage is the most common cause of stillbirth or death within the first few days.

SUMMARY

Realizing the high maternal and fetal mortality and morbidity incident to the promiscuous use of the obstetric forceps, I can only plead for less interference in the normal process of labor and the reservation of instrumental delivery for those cases presenting an absolute indication.

A PRELIMINARY REPORT ON THE USE OF BARBITURATES WITH ETHER BY RECTUM*

CLIFFORD B. LULL, M.D., PHILADELPHIA, PA.

(From the Philadelphia Lying-In Maternity Department of the Pennsylvania Hospital)

ONE of the major problems which has always confronted the obstetrician has been the relief of pain during the first and second stages of labor. Many procedures have been enthusiastically endorsed by various men during the past few decades only to be discarded entirely or modified in some manner because of their harmful effect on the mother and child, or because their analgesic power when tried on a large series of cases has been found wanting. The relief of pain in any illness has been one of the chief functions of the practitioner of medicine, and ever since the advent of twilight sleep for the relief of the pain of childbirth, has been one of the important topics of conversation among the laity, and the subject of much literary effort on the part of writers for sundry journals of both good and bad repute.

It is not the purpose of this very short paper to review the many methods that we have used for the relief of pain during labor. During the past year we have had presented a paper on the use of sodium amytal, in which are reviewed the other methods in vogue. I believe that we have no method which in every case gives complete relief from the pains of childbirth. It is therefore important that we continue to investigate all methods suggested.

The most used medication has been morphine and scopolamine in various doses. Following the suggestion of Gwathmey, many of us have used morphine with magnesium sulphate hypodermatically, followed by the instillation into the rectum of ether in olive oil. Some men have found this to be exceedingly satisfactory in their hands, reporting good results in as high as 90 per cent of cases. I do not disagree with these authorities, but must confess that in my own hands it has not been so satisfactory, although we have in selected cases continued its use. The barbituric acid preparations have grown increasingly in popularity as sedatives in the past few years and it remained for Axelrod of Cleveland to suggest the combination of the barbiturates with ether by rectum as an analgesic in labor. This seemed to be a rational outcome of our experience with the Gwathmey technic and the use of sodium amytal both by mouth and intravenously. Axelrod reports a large series with exceptionally good results, so that it was thought advisable on the Vaux Service at the Lying-In Hospital, to try this method for the relief of the pain of childbirth.

*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

The preparation used contains ethyl (one methyl-butyl) barbituric acid, 8 grains; neonal, 5 grains; quinin alkaloid, 20 grains; ether, 2½ ounces; and mineral oil 1½ ounces. The dose is given according to the body weight of the individual, the preparation coming in four ounce containers. The entire four ounces is given to the patient weighing more than 130 pounds; if the weight is less than 130 pounds, the dosage is given accordingly. There are no preliminary hypodermics of morphine or magnesium sulphate.

The contraindications to its use are upper respiratory infections, toxemia, diabetes, nephritis, and auditory disturbances.

The proper time for giving the injection is when the labor is definitely established, with good contractions occurring at least every five minutes, and the cervix beginning to dilate. It is not necessary for the dilatation of the cervix to be advanced to the extent it is advisable in using the Gwathmey technic, as we have had no case, even when given with one finger dilatation, that the labor has stopped.

The method of injection is by a small rectal tube with glass funnel. A small amount of mineral oil is allowed to run in first. The medication is then given followed by another small quantity of either mineral oil or olive oil. The usual precautions as in giving any rectal instillation are carried out. The external parts are thoroughly lubricated. The instillation is given very slowly. The patient is cautioned not to bear down, and pressure is made over the rectum when a contraction occurs. It should take approximately fifteen minutes to give the entire amount. The patient is still kept on her side and pressure made over the rectum for at least a half hour after the injection is given. We have all found in the use of any medication of this kind by rectum, that a great deal depends on the person giving it understanding what should be done, and therefore, in our work at the Lying-In Hospital, only two persons have given these instillations, namely, the day and night anesthetist. We believe rectal analgesics of any kind will have a large percentage of failures if allowed to be given by any nurse who happens to be on duty at the time and who has never had any experience with this method of medication.

Further precaution should be made after giving this medication by not leaving the patient alone at any time after it takes effect. We not only have insisted on having a nurse with the patient at all times, but have constructed a bed similar to a baby's crib, with laticed sides so that if the patient becomes restless, there is no danger of her falling out of bed.

Furthermore, these patients have to be watched more carefully because we have found in several instances the labor has progressed very rapidly, and the patient might deliver herself without being properly prepared.

Although this preparation has been used in more cases than are reported in this series, the first 50 cases only are included in this report as final conclusions have not been drawn, and will not be until a larger series have been given.

This preliminary report is now made to call your attention to this method as it seems to be worth while using.

Parity.—In this group of 50 patients, 39 were primiparae and 11 multiparae. These were not selected cases particularly, in order to give this medication to primiparous individuals, but just so happened that the majority admitted on the Service were having their first child. We have found however, in our very limited experience, that the primiparous individual seems to retain the analgesic better and seems to get more relaxation than the multipara. This is probably due to the fact that the pains in the primiparae are not as active and there is less tendency for the membranes to

be bulging through the cervical canal. Furthermore, the sphincteric control of the rectum is better in a woman who has never had a child.

Time of Giving Analgesia.—Thirty-eight patients were given the rectal instillation when the cervix was partially effaced and 2 fingers dilated; 7 patients were given it when the cervix was completely effaced and 3 fingers dilated, and 5 patients were given the rectal injection when only 1 finger dilated. As no case ceased to have contractions after the injection, we have continued to give it earlier than we did at first, and there has been no case in this series where labor was definitely established where the contractions of the uterus ceased after it was administered. I believe that this is one of the favorable points in the use of this method, in that it can be given earlier than most sedatives can be used.

Type of Delivery.—Forty-one cases were delivered by low forceps; 2 were delivered by decomposition of the breech, and 7 delivered themselves spontaneously. All the cases that were delivered by forceps or breech extraction had ether inhalation to complete the second stage. We have for a number of years delivered most of our primiparae by low forceps under general anesthesia, and we have also delivered our breech cases by decomposing them after the cervix is dilated. Some of these patients delivered by low instruments would have unquestionably delivered themselves if allowed to go on, but we have found that even though the patient had been given this rectal preparation, there was no contraindication to giving a small amount of ether by inhalation in order to keep the patient completely quiet during the delivery. We have found that the breech cases, when this analgesia has been given, are not conscious enough to cooperate in order to deliver themselves spontaneously, and therefore we have continued our usual routine method of delivery. The patients who were delivered spontaneously had no further anesthesia and none of them remember any pain at the time of delivery.

Results.—All mothers made uneventful recoveries. One or two complained of some burning about the rectum for a day or two after delivery, and one patient was reported as being incontinent for forty-eight hours. All children were born alive; cried immediately after delivery, and seemed to have suffered no harmful effect from either the rectal instillation or the addition of inhalation anesthesia for forceps delivery. Four patients bled a trifle more than normal, although not enough to warrant packing of the uterus or to call the bleeding a definite postpartum hemorrhage.

Action of Analgesia.—It was definitely stated in 42 of these 50 cases that good analgesia had been produced. In other words, in order for us to consider that we had a good result from the injection, patients were quiet, did not complain of pain and did not remember after delivery, what had taken place. When I say that patients were quiet, I mean they were not throwing themselves about the bed or noisy. The usual action was for the patient to move when the uterus would contract, but immediately doze off into deep sleep when the contraction ceased. Even when the head was on the pelvic floor, there would be no unusual action upon the part of any one of these patients, but there were only a few of these 42 who were awake enough to cooperate in bearing down at the end of the second stage. Three patients were reported as having fair results. By fair results we felt that they had some relief from pain but were not relaxed enough to be unconscious of their surroundings, and knew at all times what was going on. One patient became exceedingly irrational and noisy and had to be restrained in bed with a great deal of difficulty. This was a primipara with a long drawn out labor and continued to be irrational until after delivery. Three other patients got no result from the analgesia because they expelled the injections within a half hour after it was given. What happens in these cases is that the injection is retained for fifteen minutes, when it usually becomes effectual. Within a half hour it was expelled without the patient knowing what was happening and within twenty minutes later these patients were perfectly conscious and continued to be so during the rest of their labor. These all occurred in multiparae.

One patient retained the analgesia but got no relief whatever from her pain. She was at no time relieved of pain and remembered everything that happened from the beginning of labor.

Duration of Analgesia.—The shortest time after the injection was given before delivery was forty-two minutes, and the longest time eleven hours and fifty minutes. Most of the cases in which we report good results were really not awake for several hours after their return to the Ward, and one patient was aroused with difficulty for a period of eighteen hours.

SUMMARY

1. We do not feel that our conclusions can be final at the present time, but the results have been satisfactory enough to warrant the continued use of these drugs for a further time.

2. This method of sedation can be given earlier in the course of labor than most methods in vogue up to the present time.

3. Primiparous patients seem to respond more definitely than do multiparous.

4. If one uses this procedure, he should be prepared to deliver the patient with outlet forceps at the termination of the second stage of labor.

5. There is no contraindication to giving inhalation anesthesia to complete the delivery.

6. There has been no harmful effect upon the mother or the child.

7. These patients should be watched carefully at all times following the injection.

8. The injection should be given by a person who is particularly trained in the administration of rectal medication.

9. There was no evidence of the child suffering from either the injection of the drugs or the small amount of inhalation anesthesia given to the mother at the end of the second stage.

10. Relaxation of the pelvic muscles seem to be better than under ordinary circumstances.

11. There is a tendency, we believe, for slightly more bleeding than normal, but this has not been definitely proved.

12. Protection of the buttocks and the perineum, particularly as small amounts of material is expelled, should be carefully done.

13. Patients given this instillation can not be depended upon to cooperate during the second stage of labor because if not entirely unconscious, are mentally confused to the point of being irrational.

14. The contraindications as listed above should be particularly stressed, and especially toxemia where the amount of liver damage is not definitely known, as the therapeutists tell us that the barbituric acid preparations are eliminated principally through this organ.

15. In our limited experience this method of analgesia has proved satisfactory enough and not fraught with any danger, so that we will continue its use until a larger series has been collected.

1731 PINE STREET.

(For discussion, see page 940.)

TEMPORARY STERILIZATION BY THE INJECTION OF HUMAN SPERMATOZOA. A PRELIMINARY REPORT

M. J. Baskin, M.D., Denver, Colo.

(From the Department of Gynecology, University of Colorado, School of Medicine and Hospitals)

THE possibility of immunization of females by injection of spermatozoa is not new. It is only recently, however, that experimental work has been directed with the view of determining the practical application of such an immunization on animals and human beings.*

* * * *

From the extensive literature, although somewhat contradictory, we may draw the following conclusions:

1. Immunization is possible by injection of spermatozoa.
2. This immunization is specific for tissue and species, noting exceptions, ram and bull.
3. Large quantities of antigen are necessary for active immunization.
4. The immunization is apparently harmless and varies with the amount injected.

On this basis we began in April, 1929, the injection of human females with male spermatozoa. Our first case is then over two years old. The technic employed has been the same in all cases. Twenty women have been injected.

We are not attempting to draw any but the most general conclusions. Some of our cases are too recent to judge. We know there are a number of things to be worked out, but certain conclusions naturally follow from these. The technic has been as follows: Intercourse per condom. The specimen was tied and brought to the office as soon as possible. One cubic centimeter of hexylresorcinol was added. The entire amount was drawn into a syringe and injected into the buttocks. No semen was used with a count of less than 80,000,000 per cubic centimeter; three injections given seven days apart. The amounts of semen varied from 2 to 5 c.c. It is, of course, impossible to standardize a procedure with varying amounts. The exact amount necessary and number of injections will have to be determined by further work. Three cubic centimeters was the average amount, so that it may be stated that at least 9 c.c. were injected in every case, except one. The largest amount injected was 14 c.c. of semen.

One week following the last injection the serum was tested and tests were run every three months. The injections produced no constitutional symptoms. Local pain of moderate degree was present for about twenty-

*For lack of space the author's extended review of the literature is omitted from the Journal, but will be available in his reprints.

four hours after the first injection. There is markedly less after the second injection and after the third injection there is practically no pain.

The immunized serum was examined as follows: Three slides were prepared. One with human spermatozoa, one with spermatozoa to which nonimmunized blood serum was added, and one with human spermatozoa to which immunized serum was added. Slides were examined every fifteen minutes. In no case was there noted any delay in motility with the normal serum. The spermatozoa in these slides lived as long as in those to which no serum had been added. Under the conditions in our laboratory where spermatozoa were examined, sperms lived more than six hours if they had not been chilled. They were not examined after that time. Cervical secretions were also tested against sperms in every case.

CASE 1.—Aged twenty-five, 2 pregnancies.

Injected April 7, 14, 21, 1929, total 9 c.c.

1 wk. Sperms dead 30 min.
3 mo. Sperms dead 30 min.
6 mo. Sperms dead 45 min. All controls alive 6 hr.
9 mo. Sperms dead 2½ hr.
12 mo. Sperms dead 4 hr.

Cervical secretions negative at every examination.

Reinjected May 2, 9, 16, 1930, total 9.5 c.c.

1 wk. Sperms dead 30 min.
3 mo. Sperms dead 30 min.
6 mo. Sperms dead 30 min. All controls alive 6 hr.
9 mo. Sperms dead 45 min.
12 mo. Sperms dead 45 min.
15 mo. Sperms dead 45 min. (Aug. 1931)

Cervical secretions negative throughout.

CASE 2.—Aged thirty-nine, 4 pregnancies.

Injected June 2, 9, 16, 1929, total 11 c.c.

1 wk. Sperms dead 45 min.
3 mo. Sperms dead 45 min.
6 mo. Sperms dead 75 min. All controls alive 6 hr.
9 mo. Sperms dead 2 hr.
12 mo. Sperms alive 6 hr.

Reinjected July 3, 10, 17, 1930, total 11.5 c.c.

1 wk. Sperms dead 30 min.
3 mo. Sperms dead 30 min.
6 mo. Sperms dead 60 min. All controls alive 6 hr.
9 mo. Sperms dead 60 min.
12 mo. Sperms dead 90 min.

Cervical secretions negative throughout.

CASE 3.—Aged twenty-two, 1 pregnancy.

Injected December 7, 14, 21, 1929, total 9.5 c.c.

1 wk. Sperms dead 75 min.
3 mo. Sperms dead 75 min.

6 mo. Sperms dead 75 min. All controls alive 6 hr.
9 mo. Sperms dead 2 hr.
12 mo. Sperms dead 2 hr.
15 mo. Sperms alive 6 hr.
Cervical secretions killed sperms instantly on two examinations, 3 mo. and 9 mo. All other examinations with cervical secretions negative.

Reinjected June, 1931, total 12 c.c.
1 wk. Sperms dead 15 min.
Cervical secretions negative.

CASE 4.—Aged thirty-six, 5 pregnancies.
Injected January 4, 11, 18, 1930, total 11.5 c.c.
1 wk. Sperms dead 75 min.
3 mo. Sperms dead 75 min. All controls alive 6 hr.
6 mo. Sperms dead 3 hr.
9 mo. Sperms alive 6 hr.
Cervical secretions negative. Patient lost track of.

CASE 5.—Aged thirty-three, 3 pregnancies.
Injected March 10, 17, 24, 1930, total 14 c.c.
1 wk. Sperms dead 30 min.
3 mo. Sperms dead 30 min.
6 mo. Sperms dead 30 min. All controls alive 6 hr.
9 mo. Sperms dead 60 min.
12 mo. Sperms dead 90 min.
15 mo. Sperms dead 2 hr.
Cervical secretions negative.

CASE 6.—Aged thirty-seven, 3 pregnancies.
Injected March 15, 22, 29, 1930, total 12 c.c.
1 wk. Sperms dead 15 min.
3 mo. Sperms dead 15 min.
6 mo. Sperms dead 15 min. All controls alive 6 hr.
9 mo. Sperms dead 30 min.
12 mo. Sperms dead 30 min.
15 mo. Sperms dead 90 min.
Cervical secretions negative.

CASE 7.—Aged thirty-two, 4 pregnancies.
Injected May 2, 9, 16, 1930, total 13.5 c.c.
1 wk. Sperms dead 30 min.
3 mo. Sperms dead 45 min.
6 mo. Sperms dead 45 min. All controls alive 6 hr.
9 mo. Sperms dead 2 hr.
12 mo. Sperms alive 6 hr.
Became pregnant June, 1931, cervical secretions negative.

CASE 8.—Aged twenty-nine, 3 pregnancies.
Injected May 6, 13, 20, 1930, total 11.5 c.c.
1 wk. Sperms dead 15 min.
3 mo. Sperms dead 15 min.
6 mo. Sperms dead 45 min. All controls alive 6 hr.
9 mo. Sperms dead 45 min.
12 mo. Sperms dead 90 min.
15 mo. Sperms dead 4 hr.
Cervical secretions positive at 6 mo. examination only.

CASE 9.—Aged thirty-six, 4 pregnancies.
Injected December 2, 9, 16, 1930, total 9.5 c.c.
1 wk. Sperms dead 45 min.
3 mo. Sperms dead 60 min. All controls alive 6 hr.
6 mo. Sperms dead 90 min.
9 mo. Sperms dead 3 hr.
Cervical secretions negative.

CASE 10.—Aged twenty-four, 1 pregnancy.
Injected January 4, 11, 18, 1931, total 11 c.c.
1 wk. Sperms dead 15 min.
3 mo. Sperms dead 15 min. All controls alive 6 hr.
6 mo. Sperms dead 15 min.
9 mo. Sperms dead 60 min.
Cervical secretions positive. (Killed sperms 5 min. at first examination and 9 mo. examination.) Negative at other examinations.

CASE 11.—Aged twenty-three, 1 pregnancy.
Injected February 5, 12, 19, 1931, total 12.5 c.c.
1 wk. Sperms dead 15 min.
3 mo. Sperms dead 15 min. All controls alive 6 hr.
6 mo. Sperms dead 60 min.
Cervical secretion positive all examinations. Killed sperms on contact.

CASE 12.—Aged thirty, 3 pregnancies.
Injected February 9, 16, 23, 1931, total 10 c.c.
1 wk. Sperms dead 30 min.
3 mo. Sperms dead 45 min. All controls alive 6 hr.
6 mo. Sperms dead 90 min.
Cervical secretions negative.

CASE 13.—Aged twenty-seven, 2 pregnancies.
Injected March 6, 13, 20, 1931, total 9.5 c.c.
1 wk. Sperms dead 30 min.
3 mo. Sperms dead 60 min. All controls alive 6 hr.
6 mo. Sperms dead 60 min.
Cervical secretions negative.

CASE 14.—Aged thirty, 1 pregnancy.
Injected April 16, 23, 30, 1931, total 11 c.c.
1 wk. Sperms dead 75 min. All controls alive 6 hr.
3 mo. Sperms dead 2 hr.
Cervical secretions negative.

CASE 15.—Aged twenty-eight, 3 pregnancies.
Injected April 23, 30, and May 9, total 11 c.c.
1 wk. Sperms dead 15 min. All controls alive 6 hr.
3 mo. Sperms dead 45 min.
Cervical secretions negative.

CASE 16.—Aged twenty-six, 1 pregnancy.
Injected May 8, 15, 21, 1931, total 10.5 c.c.
1 wk. Sperms dead 75 min. All controls alive 6 hr.
3 mo. Sperms dead 75 min.
Cervical secretions negative.

CASE 17.—Aged twenty-six, 4 pregnancies.
Injected June 11, 18, 25, 1931, total 14 c.c.
1 wk. Sperms dead 5 min. All controls alive 6 hr.
3 mo. Sperms dead 15 min.
Cervical secretions negative.

CASE 18.—Aged twenty-two, 2 pregnancies.
Injected June 14, 20, 27, and July 3, 1931, total 5 c.c.
1 wk. Sperms alive 6 hr. (4 injections)
No results. Amount probably too small.

CASE 19.—Aged twenty-two, 1 pregnancy.
Injected June 12, 19, 26, 1931, total 11 c.c.
1 wk. Sperms dead 15 min. All controls alive 6 hr.
3 mo. Sperms dead 30 min.
Cervical secretions positive (15 min.) both examinations.

CASE 20.—Aged twenty-eight, 4 pregnancies.
Injected August 22, 29, September 4, 1931, total 14 c.c.
1 wk. Sperms dead 15 min. Control alive 6 hr.
Cervical secretions negative.

It will be noted from the above cases that a definite immunity was established in all cases except one (Case 18). It is probable that this patient did not receive enough semen. The total amount injected in this case was 5 c.c. for four injections. The next smallest amount injected was 9.5 c.c. These patients showed an immunity for a number of months.

None of the above cases showed any constitutional symptoms. There were no local symptoms except soreness for twenty-four hours. One patient, not listed, developed a small abscess. As the injections were not finished, this case is not recorded. Smears in this case failed to reveal an organism and abscess healed in a few days.

No patient became pregnant while her blood showed a definite toxic principle for spermatozoa. One patient (Case 7) became pregnant one year after injection. Reinjection seems to prolong the immunity. Just how long the immunity remains after reinjection is as yet impossible to state. We have not encountered any case in which the immunity does not disappear. The question of permanent sterility does not seem likely, at least after one series of injections.

We have not been able to demonstrate any individual specificity. Repeated examinations of immunized sera against spermatozoa from other males have shown no differences.

There has been no change in course, duration or character of menses in any case. If the work of Megliavacca[32] is correct such a change might be expected, but did not occur in our cases.

The varying results with cervical secretions were puzzling. Spermatoxic properties were demonstrated at times and not at others. Close questioning disclosed the fact that where cervical secretion was positive, the patient had had an orgasm. This result is being watched further.

It is possible that cervical secretion during intercourse is spermatoxic, while the normal secretion is not.

Each individual case requires such cooperation that the method is not practical at the present time on a large scale. If it were possible to use spermatozoa of some other animal, the work would be much simplified. We are at present attempting this on animals. It may be possible to destroy the species specific properties of some animal spermatozoa.

A number of questions must be answered concerning this work. Principally among these are: first, possibility of permanent sterility; second, whether ovarian changes occur; third, whether there is any effect on future generations. We are now carrying on work in an attempt to answer these questions.

CONCLUSIONS

1. Immunization of women with human spermatozoa is possible.
2. The immunization lasts about one year.
3. Revaccination at end of year prolongs the immunity for at least another year.
4. The period of immunity and degree of immunity can be determined by the blood.
5. Spermatoxic properties of cervical secretions are not constant.
6. The injections are harmless to the patient.

REFERENCES

(1) *Metchnikoff:* Ann. de l'inst. Pasteur, 1898. (2) *Landsteiner:* Centralbl. **f.** Bakteriol. **1**: 25, 1899. (3) *DeLeslie, C.:* Comp. rend. de l'Acad. des Sc. **133**: 544, 1901. (4) *Farnum, C. G.:* J. A. M. A. **37**: 1721, 1901. (5) *Taylor, A. E.:* J. Biol. Chem. **5**: 311, 1908. (6) *Dunbar, W. P.:* Ztschr. f. Immunol. 740, 1910. (7) *Kohlbrugge, J.:* Arch. f. Entwicklugsmechn. **35**: 165, 1912. (8) *Hermann, E., and Stein, M.:* Wien. klin. Wchnschr. **29**: 177, 1916. (9) *Dittler, R.:* Munchen. med. Wchnschr. **67**: 1495, 1920. (10) *Dervieux, C. R.:* Acad. Sc. 172, 1921. (11) *Hektoen, L.:* J. A. M. A. **78**: 704, 1922. (12) *Hektoen, L., and Manly, L. S.:* J. Infect. Dis. **32**: 167, 1923. (13) *Guyer, M. F.:* J. Exper. Zool. **35**: 207, 1922. (14) *McCartney, J. L.:* Am. J. Physiol. **63**: 207, 1923. (15) *McCartney, J. L.:* Am. J. Physiol. **66**: 404, 1923. (16) *Kennedy, W. P.:* Quart. J. Exper. Physiol. **14**: 279, 1924. (17) *Kovacs, F. K.:* Am. J. Obst. & Gynec. **10**: 527, 1925. (18) *Landsteiner, K., and Levine, P.:* Jour. Immunol. **12**: 415, 1926. (19) *Castoro, R.:* Arch. di ostet. e ginec. **13**: 558, 1926. (20) *Rosenfeld, S. S.:* Am. J. Obst. & Gynec. **12**: 385, 1926. (21) *Fogelson, S. G.:* Surg. Gynec. & Obst. **42**: 374, 1926. (22) *Oslund, R. N.:* J. A. M. A. **86**: 1755, 1926. (23) *Kostromin, N. E., and Kartasher, P. N.:* J. Mikrobiol. pat. i infekt. boliez. **4**: 1, 1927. (24) *Babadagly, A.:* Odessky med. j. **2**: 65, 1927. (25) *Landsteiner, K., and Van der Scheer, J. L.:* Proc. Soc. Exper. Biol. & Med. **25**: 140, 1927-28. (26) *Pommerenke, W. T.:* Physiol. Zool. **1**: 1, 1928. (27) *Babadagly, A.:* Siglo Med. **82**: 211, 1928. (28) *Jarcho, J.:* Am. J. Obst. & Gynec. **16**: 813, 1928. (29) *Levine, T. A.:* Vrach. dielo. **12**: 328 and 409, 1929. (30) *Mudd, S. N., and Mudd, E. B. H.:* J. Immunol. **17**: 1: 39, 1929. (31) *Fulconis, H., and Chiaponni, L.:* Rev. franc. de gynéc. et d'obst. **25**: 441, 1930. (32) *Megliavacca, A.:* Boll. d. Soc. Med., chir. di Pavia **44**: 433, 1930.

425 Republic Building.

THE SLOWING OF THE FETAL HEART AND ITS RELATION TO THE FETAL-PLACENTAL CIRCULATION*

MORRIS LEFF, M.D., NEW YORK, N. Y.

THE importance of auscultating the fetal heart during labor is well recognized. When the rate drops below 80 during a pain and does not return to above 100 in the interval, it is a sign of imminent danger to the child. While we have learned from clinical experience its significance, the mechanism that causes this slowing of the fetal heart is rather obscure.

A number of theories have been offered at various times to account for this occurrence. Two of them are generally accepted as explaining this condition.

Schultze, in 1871, claimed that during a strong contraction the blood supply to the uterus is interfered with, the placenta compressed, and its circulation disturbed. Proper oxygenation of the fetal blood does not occur and an excess of CO_2 accumulates, which stimulates the vagus and thereby slows the fetal heart.

The other theory is that strong pressure on the fetal head increases intracranial pressure and thereby causes the slowing.

The assumption that a strong uterine contraction interferes with the uterine circulation is not tenable. During pregnancy there is an increase of fat and muscle tissue in the uterus, which serves to protect the blood vessels from undue pressure. This is evident from the fact that after delivery, when the uterus is empty, it is reduced in size and remains contracted, yet there is no shutting off of the blood supply in the uterus sufficiently to interfere with its circulation. The contraction of the uterus and placenta no matter how severe, would not hinder the exchange of gases between the uterus and placenta, as long as the placenta remains attached.

Assuming that CO_2 is the factor which slows the fetal heart, we must consider the duration of time that the placental circulation would have to be obstructed in order to have sufficient CO_2 accumulate to act as a stimulant. A moderate slowing of the fetal heart occurs promptly with every contraction of the uterus; and the same mechanism which causes this normal slowing also produces the pathologic slowing. The normal slowing occurs so promptly with each pain, that there cannot be any accumulation of CO_2 in that instant. Even with a severe contraction sufficient time does not elapse to make any appreciable difference in the amount of CO_2. We know that in breech deliveries when the cord is completely compressed by the aftercoming head, it takes a considerable time before sufficient CO_2 accumulates to stimulate the respiratory center. Therefore it is unlikely that every time there is a contraction,

*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, May 24, 1932.

whether ordinary or severe, there is an increase of CO_2 in sufficient quantity to disturb the fetus.

The entire theory rests on the assumption that CO_2 acts as a vagus stimulant. There is no evidence however that CO_2 has any direct influence on the vagus. Consequently all the explanations of how CO_2 is produced during a contraction are irrelevant. Carbon dioxide is definitely a respiratory stimulant. Whenever there is an increase of CO_2, the respiratory center is stimulated. When the baby is born, the separation of the placenta causes the accumulation of CO_2 which starts respiration. Any intrauterine increase of CO_2 would cause the baby to breathe, rather than a slowing of the fetal heart.

It is therefore evident that the theory of an increase of CO_2 as a cause of slowing of the fetal heart should be discovered.

The objections to the theory that pressure on the fetal head produces slowing of the fetal heart are well stated by Seitz as follows: The pressure on the head during a pain is no more than the pressure on the rest of the fetus. The blood supply to the brain is abundant and is therefore not deficient during a compression. In cases of cerebral hemorrhage, meningitis, and other conditions where we know that the intracranial pressure is increased, the heart does not slow down to such an extent as it does in the fetus during a labor pain. He also claims that compression of the head with forceps does not slow the fetal heart, but accepts the theory of increased CO_2 as producing the slowing.

Baumm, Sachs, and Seitz while they accept one or both theories, quote numerous cases where the slowing of the fetal heart or the death of the fetus could not be accounted for by either of the two explanations.

The mechanism which causes the fetal heart to slow down, appears to me, to be produced as follows: We know that the same blood circulates in fetus and placenta. The total volume is about 400 c.c. and is maintained at a definite pressure in both.

When a uterine contraction occurs, the placenta is compressed and a variable amount of blood from the placenta is forced out of it into the fetus. This increases the quantity of blood in the fetus, raises the pressure in the fetal circulation and thereby causes a slowing of the fetal heart. That an increase of blood volume and blood pressure produces a slowing of the heart is a known physiologic fact. It is in accordance with "Marey's law," which states that the pulse rate varies inversely as the blood pressure. This should also apply to the fetal circulation. When the uterine contraction subsides and the pressure on the placenta is relieved the excess blood flows back into the placenta, the tension is reduced and the fetal heart returns to its normal rate.

When, however, the uterine contractions become very strong, there is an exaggeration of this process. More blood is forced into the fetus than with a normal contraction, there is therefore a greater slowing of the heart, and as the contraction lasts longer, the slowing persists for a greater time. Even when the pain is over the uterus does not relax en-

tirely, the excess blood does not return altogether to the placenta, so that the fetal heart does not return to its normal rate. When however the uterus does relax and the tension is relieved; the heart returns to its usual pace and the condition is normal again. But when the strong contractions persist, and before the heart has had a chance to recover its normal rate another contraction occurs, and more blood is forced into the fetus, the tension is further raised, the heart is still further slowed, it becomes distended, and if this continues the heart dilates and then stops entirely. It is, as if the fetus continued to be transfused with an excess of blood. To use a term applicable in this motor age, we would say that the heart stalls from being overloaded.

When the membranes have ruptured the uterus is reduced in size and the placenta is compressed. The placenta therefore cannot hold as much blood as before and the fetus must carry a greater share. With each pain the placenta is further compressed, and to a greater extent than when the membranes are intact, so that the fetal heart is more apt to be slowed after the membranes had ruptured.

When ether or chloroform is administered to the woman the uterus relaxes, the pressure on the placenta is relieved, the tension in the placenta and fetus is reduced, and the fetal heart returns to normal. If the baby is delivered the pressure is removed and the child is saved providing the fetal heart has not been overstrained nor has any hemorrhage occurred in the fetus in the meantime, as a result of this increased tension.

The increased blood volume which slows the fetal heart also causes a congestion of all fetal organs. The splanchnic area gets a large part of it. This produces a congestion of the bowels which sets up peristalsis and causes the escape of meconium. It is therefore evident why the passage of meconium and the slowing of the fetal heart are concomitant events, since they are both produced by the same force. When meconium is noticed, it is evidence that there had occurred an overloading of the fetal circulation which is apt to be repeated. The heart sounds under the circumstances need extra watching.

This increased tension in the fetal circulation, also may cause ruptures of the blood vessels in the fetus, particularly those in the brain. The tension in the blood vessels when the uterus contracts is enormous, as can be demonstrated when the cord is cut without tying. This will explain how the fetus sustains a cerebral hemorrhage in a spontaneous delivery, without any undue pressure on the head from the outside. The other hemorrhagic lesions of the fetus which are attributed to asphyxia, are produced by the increased volume of blood and increased pressure during a severe contraction.

T. R. Ford and others have produced asphyxia in experimental animals, and have shown that hemorrhages do not result from it, regardless of the degree of asphyxia. Cerebral hemorrhage in the newborn can cause asphyxia, but asphyxia does not produce hemorrhages.

In prolapse of the cord, when the cord is compressed completely, and the circulation is entirely shut off, the respiratory center is stimulated by the accumulation of CO_2, and as respiration is impossible the fetus suffocates. But usually the pressure on the cord is not complete, and a different process then takes place. The force of a uterine contraction increases the tension in the cord and enables it to withstand the pressure; so that blood is forced into the fetus. The blood cannot return to the placenta as the systole of the fetal heart is unable to overcome the obstruction. The fetal circulation therefore becomes overloaded, the heart rate becomes slower and slower, and if the condition is not relieved the heart dilates and stops.

The question arises why in certain cases a serious slowing of the fetal heart occurs, while in other cases with apparently equally strong pains, there is no effect on the rate. It must depend on several factors; first, the location of the placenta; second, the size of the placenta; third, the volume of blood in the placenta and fetus. When the placenta is located at or near the fundus in the most contractile part of the uterus, it will be compressed to a greater extent than when it is located in the lower portion. Hence more blood will be forced out of it during a pain, and a slowing of the heart will occur. If the placenta is disproportionately large it will hold a larger quantity of blood, and a greater amount of blood will be forced out of it during a contraction than from a smaller placenta, and an overloading of the fetal heart will occur. Or there may be a plethoric condition of the fetus and placenta, the volume of blood in both being large, in which case the fetus is unable to stand the extra supply which it gets from the placenta during a contraction. These conditions we cannot fortell nor can we change them. All we can do is to be on a constant lookout for a slowing of the fetal heart.

The last supposition suggests an explanation for those cases where the fetus dies at the very onset of labor. The fetus continues to develop normally during pregnancy, but with the onset of labor pains the fetal heart stops. This condition frequently is repeated in several pregnancies in the same patient. At autopsy no pathologic lesions are found. A prolapsed or twisted cord is assumed to be the cause of these deaths but usually none is found to account for it. What happens is similar to the condition mentioned above. Due to some factor in the development of the fetus an excess of blood is produced, which is the maximum the fetus and placenta can hold. At the onset of labor with the first contraction, the heart is overloaded and the fetus succumbs. In a patient that has had this unfortunate occurrence repeated, elective cesarean section saves these babies by preventing the overloading of the fetal heart. These children show no abnormalities after birth to otherwise account for their precarious intrauterine condition.

When the baby is delivered, and the heart beats very slowly, or is hardly perceptible, one method of stimulating the heart is to cut the cord without tying and allowing some blood to escape. This relieves

the overload on the heart. More effectual, is mouth to mouth respiration. By distending the baby's chest, the lungs draw in a quantity of blood which relieves the overload on the heart. At the same time the respiratory system is set in motion, the heart rate increases, and the baby continues to breathe regularly.

The sympathetic nervous system is not fully developed in the fetus, and there is no evidence of the placenta being supplied with these nerves. The question arises, how is the blood pressure in the fetus and placenta maintained? The likely explanation is that the placental and fetal circulation derives its tone from the uterus. It is the tonic state of the uterus, which holds the placenta in place and properly contracted. This contraction maintains the pressure in the placental circulation, which in turn is transmitted to the fetal circulation. Should the uterus, for some reason suddenly relax, pressure in the fetal and placental circulation would drop and the fetus would go into shock. This, I believe, explains how death of the fetus occurs when the mother suffers a sudden nervous shock. A general relaxation takes place in all abdominal viscera of the mother. The uterus loses its tone and relaxes, this removes the tone from the placenta and the vessels dilate. The blood from the fetus flows out of it into the placenta, the blood pressure drops, and the fetus goes into shock and dies.

SUMMARY

The accepted theory that the slowing of the fetal heart is produced by an interference with the oxygenation of the fetal blood and consequent increase of CO_2, which stimulates the vagus, is erroneous.

Pressure on the fetal head, also, does not explain the slowing of the fetal heart.

The slowing of the fetal heart is produced by the contraction of the uterus compressing the placenta and forcing some blood out of it and into the fetus. This increases the volume and tension in the fetal circulation which causes the heart to slow down. With a severe pain this process is exaggerated and an extreme slowing occurs.

The increased blood volume during a severe contraction also produces a congestion of the bowels, which stimulates peristalsis and causes the escape of meconium at the same time that the slowing of the fetal heart occurs.

The increased volume and tension in the fetal circulation can cause rupture of the fetal blood vessels, with hemorrhages in the brain or other organs. These hemorrhages cause asphyxia, but asphyxia does not produce hemorrhages.

In prolapse of the cord the slowing of the heart is produced by an overloading of the fetal circulation. The blood from the placenta is forced into the fetus, but the blood is unable to return to the placenta due to the compression of the cord.

Death of the fetus at the onset of labor is produced by an overloading

of the fetal heart, in those cases where there is an excess of blood in the fetal-placental circulation.

When the mother suffers a sudden nervous shock, death of the fetus is produced by a relaxation of the uterus and placenta. This causes the blood to flow out of the fetus and into the placenta, thereby producing a fatal anemia in the fetus.

REFERENCES

Baumm, P.: Arch. f. Gynäk. **107**: 1917. *Ehrenfest, Hugo:* Birth Injuries, 1931, New York, D. Appleton & Co. *Feldman, W. M.:* Child Physiology, 1920, London. *Ford, R. T.:* Bull. Johns Hopkins Hosp. **42**: 70, 1928. *De Lee, J. B.:* Obstetrics, 1928, Philadelphia, W. B. Saunders. *Marey, E. J.:* La Circulation du Sang, 1881, Paris. *Sachs, E.:* Ztschr. f. Geburtsh. u. Gynäk. **82**: 284, 1920. *Schultze, B. S.:* Der Scheintod Neugeborener, 1871, Jena. *Seitz, L.:* Zentralbl. f. Gynäk. **40**: 1916. *Stoeckel, W.:* Lehrbuch der Geburtshilfe, 1930, Jena. Gustav Fischer. *Williams, J. W.:* Obstetrics, 1930, New York, D. Appleton & Co.

15 East One Hundred Eleventh Street.

THE INDICATIONS FOR STERILIZATION*

Louis H. Douglass, M.D., Baltimore, Md.

(From the Department of Obstetrics, University of Maryland)

STERILIZATION with its indications is a subject which is constantly being brought to the attention of the busy general practicioner and the obstetrician connected with an active clinic. In spite of this there are very few references to the subjet in the Obstetrical Literature, the standard textbooks dismissing the indications with a very few lines, and devoting but little more space to the various methods. DeLee says, in effect, that any disease which is a contraindication to pregnancy is an indication for sterilization, and allows the matter to rest there. A search of independent literature is almost as barren, the most notable exception being Williams' most valuable article in the *Journal of the American Medical Association* in 1928.

The subject is one which is very much to the fore at the present time, and the only way any unanimity of opinion may ever be reached is for everyone to be perfectly frank about his own opinions and his work. In this way there will at least be a basis for argument and something from which those with more limited experience may draw conclusions.

In the past eleven years at the University Hospital, sterilization has been considered necessary or advisable in 55 instances. Since 10 of these were Porro sections, in which infection was the indication in 6 cases, obstructive tumors in 2, and abruptio placentae and cervical carcinoma (really a panhysterectomy) in 1 each; the operation was intentional 45 times. There occurred in the clinic over this same period 20,458 deliveries, giving a sterilization incidence of 1 in 454 deliveries.

*Read before the Obstetrical and Gynecological Section of the Baltimore City Medical Society, January 15, 1932.

The indications are several and the methods used vary somewhat and our views and results are offered with the hope of stimulating discussion and prompting others to report their experiences also.

INDICATIONS

Incidental Group (Porro operations)		
1. Prolonged labor with infection	6	
2. Obstructive tumors	2	
3. Abruptio placentae	1	
4. Carcinoma of cervix (panhysterectomy)	1	
Intentional Group		
1. Cephalopelvic disproportion with repeated sections, 3 or more	17	37.7%
2. Nephritic toxemia with multiparity	7	15.5%
3. Heart conditions complicating pregnancy	6	13.3%
4. Low mentality (repeated pregnancies with mentally defective children)	6	13.3%
5. Epilepsy	3	6.6%
6. Placenta previa and multiparity	2	4.4%
7. Chorea	2	4.4%
8. Tuberculosis, pulmonary	2	4.4%
Total	45	100. %

Of the 10 cases in which the uteri were removed, the 6 done for infection all occurred before the extensive use of laparotrachelotomy, and were they to come under our care today, it is probable that this would be the procedure in most of them. The remaining 4 need no comment other than that it is surprising that we have not found it necessary to remove more uteri for abruptio placentae.

(Our noncorrected maternal mortality for this condition over the period covered by this report is 6.85 per cent.)

Of the 45 cases in the intention group, 17 were done because of cephalopelvic disproportion, all of the patients having had 2 or more cesarean sections prior to the one accompanied by sterilization. It seems unfair to expose the mother of a family of this size to the dangers of further pregnancies and operations.

Next in order of frequency is nephritic toxemia with 7 instances, then heart conditions and low mentality, 6 of each.

The cases of nephritic toxemia were all cases which we had cared for repeatedly in our Clinic and in which evidence of increasing kidney damage had been noted with successive pregnancies. To merely carry a case of this kind through her pregnancy, to deliver her of a premature child, either stillborn, weak or puny, with little chance of surviving, and to discharge her with the warning that she must not become pregnant, is to treat her very inadequately. The present status of the various contraceptives is such that they are of little or no value to the clinic type of patient, and of not much more to anyone. So that if pregnancy is very evidently contraindicated, there is little else to do other than to sterilize.

Of the heart conditions which were deemed sufficiently grave to warrant sterilization, 4 were primiparae, 1 a para ii and 1 a para iii. They had all suffered decompensation at one time or another, and none probably should

have become pregnant at all. Pregnancy having occurred, however, it did not seem that anything was to be gained by interruption, and indeed, all of these women went through their pregnancies remarkably well, requiring very little treatment. Rest was insisted upon, and occasionally digitalis was given. Local anesthesia was used 5 times and avertin once.

The low mentality cases were all seen by consultants of the psychiatric department, they were all multiparae, and all had mentally defective children. The sterilization was not only recommended but urged by the consultants in all of these cases.

There were 3 cases of epilepsy, 2 of them primiparae, and the third a para ii, with one child, a hopeless idiot. Operation in all of these cases was also done only after psychiatric consultation.

The 2 patients with placenta previa who were sterilized were both multiparae (para xi or xii), on whom cesarean section was done because of central placenta previa, and the sterilization was more or less incidental.

One of the cases of pulmonary tuberculosis was a para ii, the first labor nine years before having been terminated by cesarean for maternal exhaustion. She had had one kidney removed two years before this for tuberculosis and after delivery her chest condition became active and she was in a sanatorium for several years, from which she was finally discharged as an arrested case. She was seen early in this pregnancy and was referred to 3 competent internists. Their consensus of opinion was that she was quiescent and that the pregnancy should be allowed to continue. Section and sterilization under local anesthesia were done at term, with very pleasing results for both mother and child. The other was a para viii with a healed tubercular lesion who was sectioned for placenta previa and sterilized at the same time. The 2 cases of chorea also exhibited a very low mentality and were obviously unfit for motherhood.

METHODS OF STERILIZATION

Unless there seemed a pathologic indication to do so, none of our cases were sterilized by hysterectomy. In 18 cases the tubes were resected and the ends buried and in 27 Madlener's technic, kinking, crushing and tying of tube, was followed. There was at first considerable criticism of this method by our own clinic members, but it has gradually subsided to a low murmur and with one exception we are now all in accord that it is simple and as safe as any in which a removal of uterus, tubes and ovaries is not resorted to.

In this connection it is interesting to note the change in attitude of one of the outstanding obstetric authorities of our country. In 1926 he stated that it might be used when time was an important element, but that he did not fully trust it. In 1927 he had begun to use it but was not ready to report upon it. In 1929 it was declared to be "almost as positive as tubal excision, if not its equal." In 1930, "one of the surest, easiest, and safest of methods." This method has the added advantage that the tube may later be reunited if desired. It readily lends itself to local anesthe-

sia, and is not complicated by any bleeding at all. We have had no failures from this method and in the literature there are remarkably few (1 in 545 cases, and 2 more without any statement as to the number of cases) so few indeed that when they do occur, an error in technic, as simple as it is, may be suspected. Of the cases sterilized by resection of the tubes, 18 in number, one later became pregnant and returned to us. She was one of the contracted pelvis series, was again sectioned and *resterilized.* The entire group of 55 offered nothing else of interest either in mortality or morbidity.

DISCUSSION

What, then, are the indications for sterilization? The list is a long one and many of the indications must, of necessity, be very elastic. The number of children already born, the desire for children, the general condition of the mother in addition to the specific indication, and many other things will all have to be considered before a decision may be reached.

When the question arises in our own clinic, we have been in the habit of referring the patient to the necessary consultants, and then when all of their opinions are at hand the case is brought up for discussion before as many members of the obstetric group as can be present. Everyone feels free to voice his opinion and after a full discussion, the question is decided.

Parenthetically it is interesting to note that since we have been doing more sterilizations, the question of the interruption of pregnancy arises less and less frequently. The case of epilepsy with one child, an idiot, was sent us for interruption. We allowed her to go to term and two years later the psychiatrists reported that the baby was apparently of normal mentality.

The kidney and heart cases have already been discussed, and need no additional comment. In tuberculosis, the internist must be listened to very closely and his advice should bear great weight. In contracted pelves, if the mother is in otherwise good condition, the procedure need not be considered until the third delivery, or under special conditions, the fourth or fifth. Cesarean section on selected cases, properly prepared and done as an operation of choice should give excellent results in competent hands.

Low mentality has given us the most concern of all the indications we have met. Many of our patients had given indications of being unfit for motherhood, and others were already the mothers of mentally defective children, and would apparently continue to bring such children into the world if nothing were done. Any contraceptive advice is of course useless in these cases, and sterilization is the only means of controlling them. Psychiatric consultation is always requested when a question of mentality arises, and the department has given us most whole-hearted cooperation, as indeed have all the other consultants we have called upon.

Only a few of the more outstanding indications have been considered

here, but I am sure that with other contributions to this subject the list will rapidly grow.

In the preparation of this paper I have carefully reviewed the cases in the series, and with the exception of the Porro sections, the most of which would have laparotrachelotomies today, I found none which in retrospect offered a weaker indication that it did at the time of operation.

If a cesarean section seems too drastic a procedure, it is a perfectly simple matter to allow labor to proceed in the usual manner and to open the abdomen during the puerperium. The sterilization may then be done by any method desired.

MEDICAL ARTS BUILDING.

REPORT OF A CASE OF RAMIFYING ANGIOMYOMA OF THE UTERUS

LEWIS C. PUSCH, M.D., RICHMOND, VA.

(From the Department of Pathology of the Medical College of Virginia)

UTERINE neoplasms composed essentially of blood vessels, or presenting blood vessels as conspicuous features, are unusual. Recently Horgan[1] reported a case and reviewed 21 cases previously reported. He separates these into four groups: (1) true cavernous hemangiomas in the wall of the uterus without fibromyomas, (2) hemangiomatous fibromyomas, (3) telangiectatic hemangiomas in the pelvis, and (4) a doubtful case of hemangioma in the cavity. Where recorded, recovery is given as the clinical result in all except one case; in this, death occurred a few days after operation. In addition, angiomyomas uteri have been reported by Mandelstamm,[2] Ehnmark,[3] Erede,[4] Neumann,[5] and Tarlo[6] during the last five years, while during the same period Brodersen[7] reported a case of angioma mucosae uteri. Frank[8] has reported a case of hemangioma of pelvic connective tissue. Still others refer to intrauterine phlebectasia of angiomatous type[9] and to proliferations of blood vessels and of lymph vessels in myometrium and myomas.[10] A complete review of the literature will not be attempted.

REPORT OF CASE

Clinical Data.—H. M., negro, aged thirty-three, single, was admitted to the surgical service of the Hospital Division of the Medical College of Virginia on August 15, 1930, complaining of pain in the lower right quadrant of the abdomen and in the lumbar region of the back. The onset had been about seven weeks previous to admission. During most of this interval the patient had been in bed. The lower abdominal pains were colic-like in character. Nausea, vomiting, and loss of appetite were associated. There had been a leucorrhea of a yellow color, which lately had disappeared. On two previous occasions there had been attacks similar to the present. The family history was unimportant.

On admission the patient was well nourished, well developed, and did not appear to be acutely ill. Pyorrhea was noted. The heart and lungs were regarded to be normal. The abdomen was not rigid and moved freely with respiration. On palpation tenderness was noted over the entire right side, most marked in the lower right quadrant. No masses could be felt. Tenderness was noted in the right lumbar region. Vaginal examination revealed a dilated soft cervix and gave an impression of fullness on the right side. The body temperature was 98° F., the pulse 80, and respirations 22.

The preoperative clinical diagnosis was chronic salpingitis with chronic appendicitis. Laparotomy was performed by Dr. Webster P. Barnes on August 18 under spinal anesthesia. There was a right indirect inguinal hernia with a piece of omentum adherent to the orifice. The fundus of the uterus had the size of a duck egg.

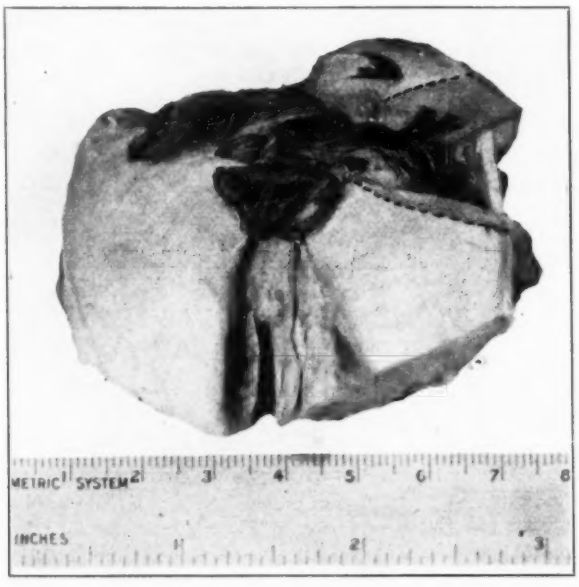


Fig. 1.—The gross specimen with ramifications of the tumor (shaded portion) bulging from cut surfaces of the fundus. The broken lines indicate edges left after removal of a wedge-shaped piece of tissue from the cornu.

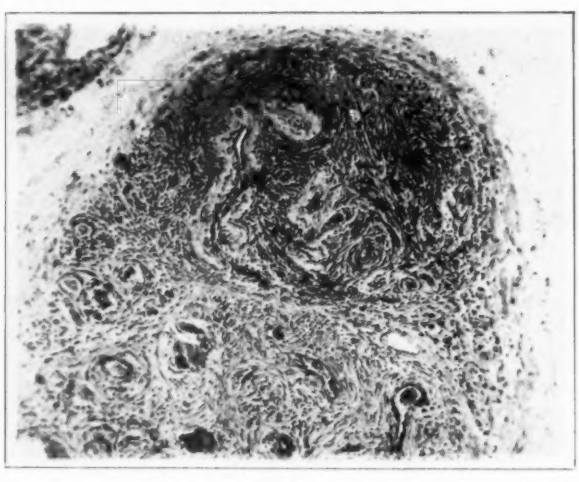


Fig. 2.—Cord-like structure of much of the tumor, with the cord shown composed of blood vessel axes having perivascular bundles of smooth muscle cells.

Adhesions bound both fallopian tubes, with numerous serous retention cysts associated with the surface of the right tube. The hernial sac was removed from within. The body of the uterus, both fallopian tubes, right ovary and appendix were removed.

The Specimen.—The specimen received consisted of the body of a uterus with both fallopian tubes and right ovary attached, a semitransparent serous retention cyst

3 cm. long, and an appendix. The fallopian tubes, thickened and edematous, presented a chronic inflammatory response. A similar reaction was less marked in the appendix. The 3 cm. cyst as well as others associated with the peritoneal surfaces of the right fallopian tube and ovary had mesothelial linings.

The body of the uterus was received incised longitudinally. In this state its dimensions were 8 cm. in superior-inferior diameter, 8 cm. in lateral diameter, and 3.7 cm. in anterior-posterior diameter. A soft pink nodule not unlike early placental tissue, 2½ × 2 × 1 cm., bulged from the cut surface of the myometrium at the fundus and occupied a portion of the exposed endometrial cavity, to which it then had access through the postoperative incision. On dissection this nodule was found to be a continuation of a branching, truncated mass of similar character, 7.5 cm. long and 0.1 to 1.5 cm. in diameter, ramifying throughout the myometrium of the fundus from cornu to cornu. It was soft and pink, separated readily from its myometrial bed, leaving a smooth surface without a definite capsule, and appeared throughout much of its course to be composed of a group of cord-like structures

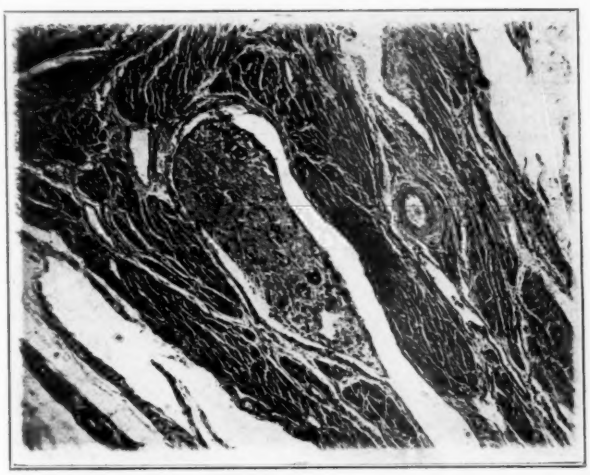


Fig. 3.—Cord of tumor tissue within a dilated vein.

having axes coinciding with those of the ramifications of the growth itself. A boggy swelling 2½ cm. in diameter at the left cornu was found to be occupied by a portion of the mass. On separating the appendages from the uterus, a soft, red, smooth, globular structure a few millimeters in diameter bulged from the cut surface of the broad ligament of the left side immediately beneath the isthmus of the fallopian tube. The peritoneal and endometrial surfaces nowhere were perforated by the growth. The endometrium was smooth, thin, and pink. The mass did not involve the lower half of the body of the uterus.

Microscopically, the branching truncated mass was composed essentially of conspicuous blood vessels which served as axes for a perivascular distribution of smooth muscle fibers. The blood vessels and surrounding muscle fibers constituted units which were grouped somewhat indistinctly into cord-like structures bordered by a loose edematous connective tissue stroma (seen in cross-section in Fig. 2). In many instances such cords, with a smooth thin mesothelial surface, occupied dilated venous paths (Fig. 3). Fusion of the neoplasm with adjacent myometrium after the manner of malignant neoplastic invasion was nowhere observed. The tissue was well differentiated. Many of the blood vessels serving as axes for the units had hyalinized walls; others were markedly dilated (Fig. 4). The muscle fibers about the blood vessels in most instances occupied a concentric relationship to the vessel; in other

instances they presented a radial arrangement. Inflammatory infiltrations of leucocytes and wandering cells were marked in some areas. The neoplastic tissue was found only in the fundus; several sections covering the circumference of the lower portion of specimen were free from the tumor.

At the present time, nearly fourteen months after operation, the patient is reported to be well and is working.

COMMENT

Superficially, the unusual ramified shape of the tumor suggests a malignant neoplasm. The ramifications, however, everywhere could be separated readily from the myometrium. For the greater part, they were not attached to their myometrial bed. Histologically, the well differentiated structure supports its benign nature. The absence of a compact circumscribed tumor and the soft pulp-like structure are unlike the usual myoma of the uterus, but not unlike an angioma. The tendency toward

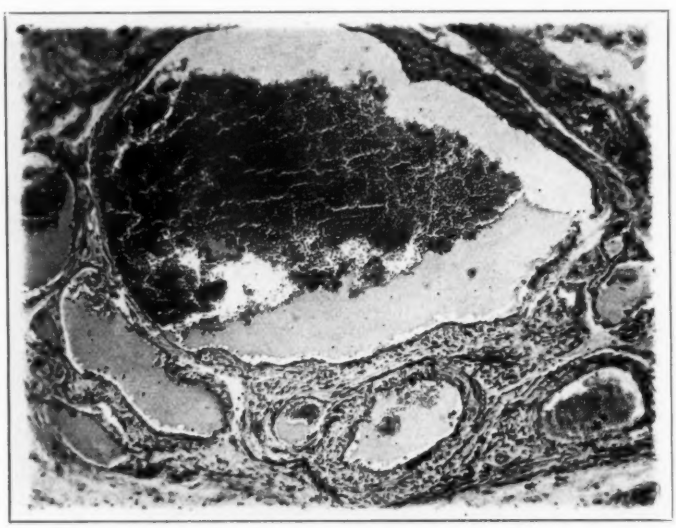


Fig. 4.—Area in which dilated blood vessels constitute the most conspicuous feature of the tumor.

intravascular growth without being adherent to the vessel wall is seen occasionally in myomas.

SUMMARY

A uterine neoplasm having an unusual ramified distribution within the myometrium, regarded to be benign, structurally consisting of cords of perivascular groups of smooth muscle cells, with the blood vessels constituting the greater part of the bulk in some areas, is recorded, occurring in a patient having bilateral chronic salpingitis, and found incidentally at an operation performed for the purpose of relieving that condition.

REFERENCES

(1) *Horgan, E.:* Surg. Gynec. Obst. **50**: 990, 1930. (2) *Mandelstamm, A.:* Monatschr. f. Geburtsh. u. Gynäk. **83**: 69, 1929. (3) *Ehnmark, E.:* Upsala Läkaref Förk. **34**: 219, 1928. (4) *Erede, U.:* Arch. di Biol. **5**: 29, 1928. (5) *Neumann, H. O.:* Arch. f. Gynäk. **131**: 50, 1927. (6) *Tarlo, B.:* J. akush. i zhensk. boliez. **38**: 306, 1927. (7) *Brodersen, N. H.:* Norsk. Mag. f. Laegevidensk. **89**: 384, 1928. (8) *Frank, R. T.:* Am. J. Obst. & Gynec. **20**: 81, 1930. (9) *Tsakona, S.:* Bull. et mém. soc. de chir. de Paris **21**: 670, 1929. (10) *Neumann, H. O.:* Arch. f. Gynäk. **139**: 161, 1929.

ADENOSARCOMA OF BODY OF UTERUS

LAWRENCE SOPHIAN, M.D., NEW YORK, N. Y.

TWO cases of an unusual variety of tumor occurred in the surgical material at the Roosevelt Hospital within a few months of one another. These were both polypoid tumors of the body of the uterus filling a considerable portion of the endometrial cavity, and in one case, dilating it very markedly. On microscopic examination both proved to be made up of a mixture of tissues including smooth muscle, myxomatous fibrous tissue, spindle-cell sarcoma, cartilage and an admixture of glands of the endometrial type but poorly developed and immature. This type of tumor was clearly described by Wilfred Shaw in 1928.[1] He collected from the lit-

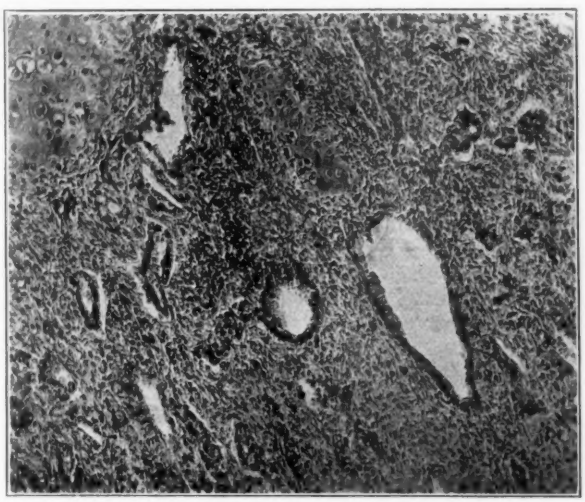


Fig. 1.—Microphotograph of Case 1 (×70). The admixture of gland-like spaces and cellular stroma containing cartilage can be observed.

erature thirteen cases, of which the earliest was reported in 1870. Shaw compared these tumors with the grape-like sarcoma of the cervix (Sarcoma botryoides), a much commoner tumor, which he found was also histologically a mixed tumor of similar composition and microscopically of the same variety. He also makes note of a third group of mixed tumors of this peculiarity of structure occurring in children in the vagina. This entire group of genital mixed tumors has a marked resemblance to the Wilms tumors of the kidney and Wilms himself in his monograph in 1900 compared the "Traubiges Sarkom" of the cervix to the mixed tumors of the kidney, considering them of similar embryonal development. The rarest of the tumors are those occurring in the body of the uterus and here, too, the age occurrence is markedly different from those occurring in the cervix or vagina. The ages given in the reported cases were as follows: 50, 49, 56, 62, 75 and 58. These cases all occurred after the menopause. Most, if not all of them, were polypoid, and Shaw considers that the structure differs from that of the cervical tumors largely because the limitation of the tumor to the endometrial cavity restricts the formation of multiple polypoid projections as in the grape-like sarcoma of the cervix. Another case of

mixed tumor of the body of the uterus was reported by Wolfe.[2] This occurred in a patient of fifty-five years, in conjunction with fibromyomas and was a polypoid tumor consisting mainly of myxomatous and cartilaginous elements. The case histories of the two examples here reported, follow:

Mrs. C. L. B., aged fifty-five, came to Roosevelt Hospital, September 17, 1930, under the care of Dr. H. C. Taylor. She had had four children, the last twenty-five years ago. In 1918 she was given radium treatment by Dr. Corscaden for an enlargement of the uterus which was considered a fibroid. After that, menstruation ceased. Her complaint on admission was backache, with some urinary symptoms, especially urgency. Operation was performed. The uterus was found much enlarged and a complete abdominal hysterectomy was done. The specimen was found to consist of a much enlarged uterus with tubes and ovaries with a combined weight of 1030 gm. On section the uterus was seen to have a much dilated cavity filled by a pedunculated mass measuring 15 by 12 by 10 cm. The surface was irregularly brown

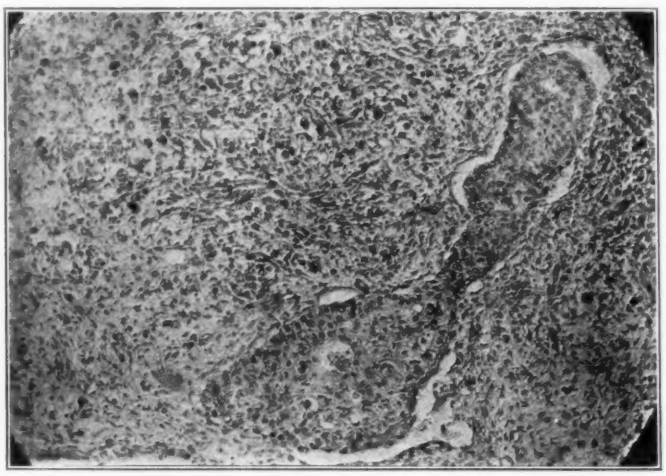


Fig. 2.—Microphotograph of Case 1 (×200). The stroma cells are large, with a mixture of round and spindle shapes. The epithelium of glands and cords is seen to be atypical. Mitotic figures are present.

and red with some erosion. The cut surface was soft, fibrous and fatty with many small cysts. A great deal of tissue was hemorrhagic and necrotic. The microscopic appearance was so similar to that of the second case that the descriptions are combined below. The postoperative course was uneventful. About six months after operation symptoms of partial intestinal obstruction developed. There was no palpable pelvic mass but the region was indurated. In spite of x-ray treatment to the pelvis, the obstruction became worse and the patient died during November, 1931. No permission for autopsy was obtainable.

The second case, Mrs. S. G., aged sixty-four, came to Roosevelt Hospital, under the care of Dr. W. P. Healy. She had had radium treatment nine years ago which resulted in menopause. In June, 1930, uterine bleeding began and continued until August. X-ray treatments were given in July and in Sepetmber. Patient was examined under ether, on October 4, 1930, and a globular uterus was felt. On curetting, fragments were removed which on microscopic examination were reported as resembling necrotic fibroid. Operation was performed February 20, 1931, with the removal of the uterus and adnexa. The combined weight was 125 gm.; the uterine lumen was enlarged, being entirely filled by a yellowish red, fungating, pedunculated growth, attached to the fundus by a firm fibrous pedicle 2 cm. in diameter. There

was no encapsulation at the attached base of the tumor. The uterine wall was about 1½ cm. in thickness and seemed normal. The adnexa were negative. The subsequent course of this patient was uneventful and in January, 1932, eleven months after operation, she reported herself free of symptoms.

The histology of these two tumors was similar in all respects. There was no evidence of encapsulation and on the border between the tumor and the uterine wall invasion seemed to be taking place rather actively. There were numerous clefts and gland spaces lined by cuboidal or columnar epithelium, characterized by a frayed inner border and vesicular nuclei. Usually one layer of epithelium was present but sometimes the epithelium was heaped up and in some of the larger spaces secondary acini were formed. This epithelium showed mitotic figures and resembled adenocarcinoma of endometrial origin. The stroma was remarkable in its variety. Most

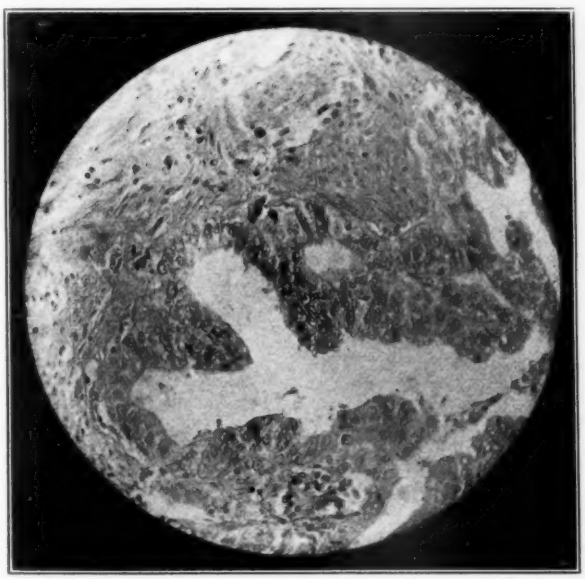


Fig. 3.—Microphotograph of Case 2 (×600). The section is through the pedicle of the tumor and the upper part of the section is myometrium which is being invaded by epithelial elements which here have the appearance of actively growing carcinoma.

frequent was a myxomatous appearance, with small cells resembling fibroblasts predominating, but in places the cells were large spindle cells often with giant nuclei, having every appearance of a rapidly growing sarcoma. In other foci the intercellular substance was of more solid consistency and small round islands of typical cartilage matrix and of smooth muscle were found. There were also large cells with eosinophilic cytoplasm and single or multiple nuclei which had the appearance of embryonal striated muscle. In some of the gland spaces a portion of the epithelium consisted of large cells with much clear cytoplasm and small central nuclei resembling keratinized epithelium.

These tumors are readily recognizable by their remarkable histologic structure and apparently form a special group which characteristically occurs in the postmenopausal period and causes enlargement of the uterus and bleeding. Apparently most of the tumors, if not all, judging by Shaw's report, are pedunculated intrauterine masses. Because of the invasive character of the growth, the malignancy must be fairly marked, and according to the previously reported cases, recurrence and metastases are to be expected. If comparison with Wilms tumors is justifiable, a

great deal should be expected of radiation therapy, since in this group, the radiosensitivity is of high degree.

REFERENCES

(1) *Shaw, Wilfred:* J. Obst. & Gynec. Brit. Emp. **35**: 498, 1928. (2) *Wolfe, S. A.:* Am. J. Obst. & Gynec. **19**: 816, 1930.

ARTIFICIAL PNEUMOTHORAX AND PREGNANCY WITH THE REPORT OF TWO CASES*

J. W. Cutler, M.D., Philadelphia, Pa.

IT IS my privilege to present the following two cases of advanced pulmonary tuberculosis who have been treated successfully by artificial pneumothorax and who went through full-term pregnancies while under treatment.

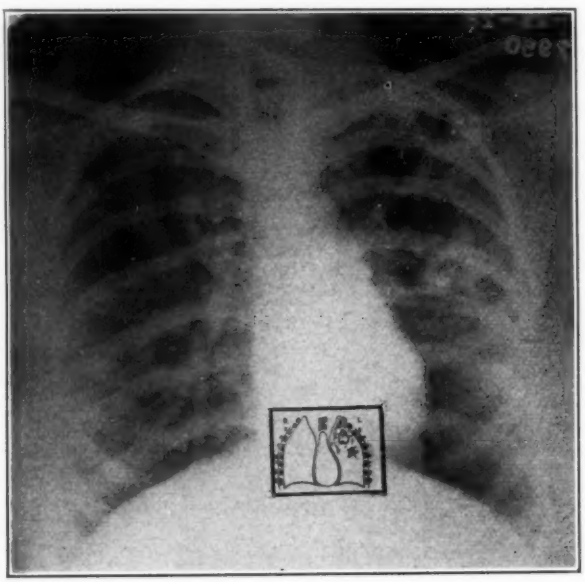


Fig. 1.—Case 1. Condition of lungs on admission to the sanatorium July 20, 1928. Infiltration, consolidation, and excavation in upper half of left lung. Sputum positive for tubercle bacilli. Note size of cavity.

Case 1.—R. S., aged twenty-two, first came under my observation at the Eagleville Sanatorium on July 20, 1928, suffering with advanced active tuberculosis of the left lung, temperature 99.8°, pulse 96, sputum positive for tubercle bacilli. Clinically there were signs of excavation in the first interspace anteriorly, with râles extending to the fourth rib. The patient also complained of nausea and vomiting with pain over the right lower abdomen, and no menses for the past two months. These symptoms, however, received little consideration at the time and were believed to be due to probable ileocecal tuberculosis. The patient was placed on calcium chloride therapy intravenously and in due time the nausea and vomiting disappeared. During the first six weeks of observation, the temperature, cough, and expectoration continued to in-

*Presented, by invitation, before the Obstetrical Society of Philadelphia, March 3, 1932.

crease in severity and the patient was losing steadily in weight. On September 1, 1928, artificial pneumothorax was instituted on the left side and almost immediately the patient began to show definite improvement. Temperature and pulse soon quieted down to normal, cough and expectoration was greatly reduced and tubercle bacilli disappeared from the sputum. The patient began to gain in weight and naturally felt greatly elated over the turn of events. On November 8, 1928, the patient called my attention to the fact that her abdomen was increased in size and made the suggestion that she was pregnant. Careful examination soon confirmed the diagnosis and for

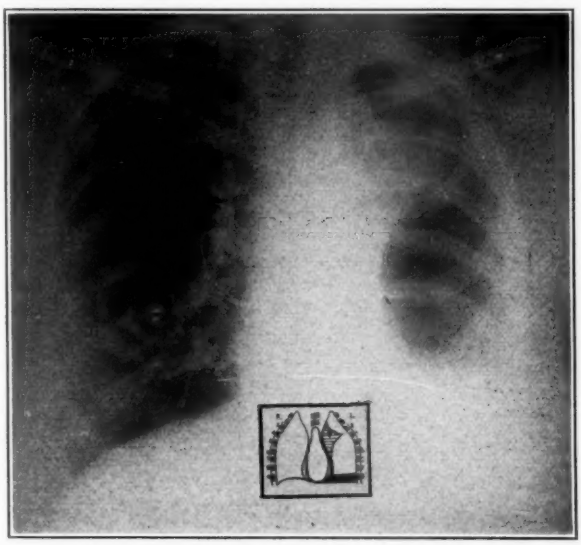


Fig. 2.—Case 1. May 8, 1929, two months after giving birth to a healthy, male child while under artificial pneumothorax treatment. Note fluid level and collapse of left lung. The cavity although greatly reduced in size is still visible. In the diagram the uncollapsed part of the left lung is represented by the shaded area, the solid area indicates fluid. Sputum negative for tubercle bacilli.

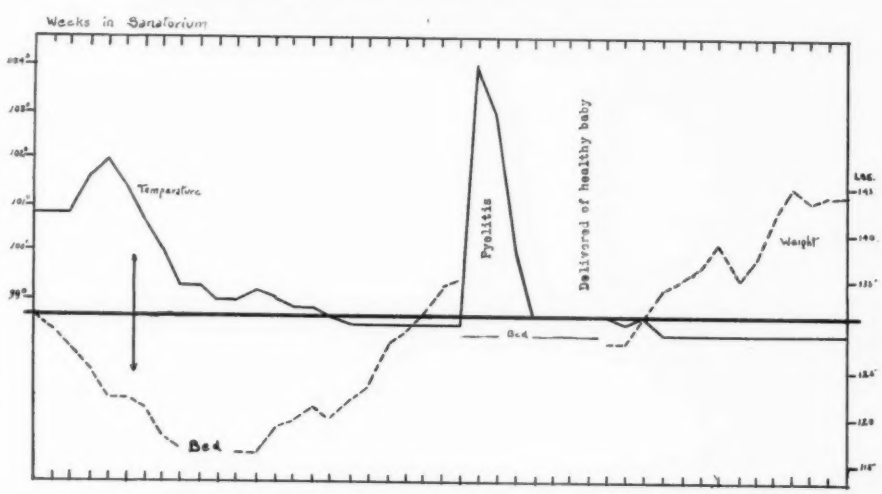


Fig. 3.—Case 1. Clinical course during stay in sanatorium. Admitted July 20, 1928, discharged July 16, 1929. Artificial pneumothorax to left lung (indicated by arrow) initiated September 1, 1928. Delivered of healthy, male child, March 4, 1929. Both mother and baby at the present time, March 24, 1932, enjoy good health. Mother still receives artificial pneumothorax treatment.

the first time it was realized that the patient was pregnant on admission and that the nausea and vomiting were not due to ileocecal tuberculosis as was first believed but to pregnancy. Of course, it was too late to interrupt gestation, and again the patient was in such splendid shape clinically, that she was advised to go through with it. Everything went along smoothly until January 10, 1929, when she suddenly developed a high fever of 104° with moderate pain in the right upper abdomen. A diagnosis of right sided pyelitis was established and the patient treated accordingly with satisfactory results. At the same time fluid appeared in the left pleural cavity which required several aspirations. On March 4, 1929, the patient delivered a healthy male child at the Jewish Hospital under the supervision of Dr. Walker. The convalescence was uneventful. Although the sputum became positive for a short time after the delivery, the tubercle bacilli again disappeared. The patient continued to gain in weight and strength and left my care as an arrested case of tuberculosis on July 16, 1929. A recent report from the patient stated that she was enjoying good health,

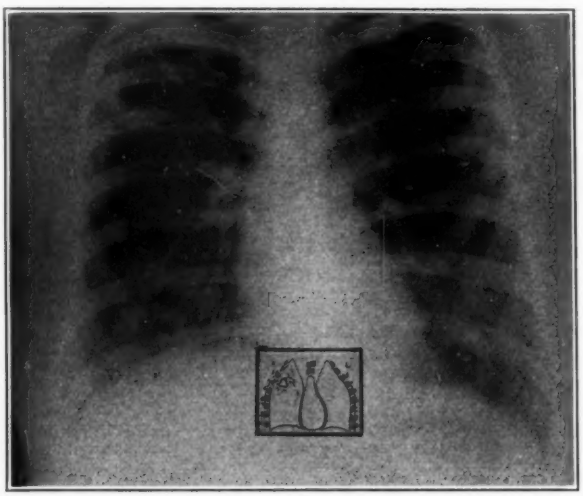


Fig. 4.—Case 2. Note the marked involvement of the right upper lobe with large cavity at the level of the fourth posterior rib. Sputum positive for tubercle bacilli.

that the baby was in fine shape, and that she was still continuing with artificial pneumothorax treatment.

It is highly probable that had I realized that this patient was pregnant when she first came under my care, she would have been aborted.

CASE 2.—I. G., aged twenty-four, first came under medical observation for tuberculosis in May, 1929, at which time she was known to be three months pregnant. Both x-ray and physical findings revealed softening and excavation of the right upper lobe. The sputum was positive for tubercle bacilli and clinically there was cough, expectoration, fever, and night sweats. During the two weeks prior to the diagnosis of tuberculosis, the patient had lost nine pounds in weight and was confined to bed. Because of the severe character and apparent acute onset of the tuberculous process a therapeutic abortion was performed on June 1, 1929, by Dr. Andrusier at the Howard Hospital, and the patient admitted to the Eagleville Sanatorium on June 14, 1929. My contact with the patient began on this date. The patient was still manifesting all the signs and symptoms of acute tuberculosis, and artificial pneumothorax to the right lung was instituted within a few days. In a short time, her temperature returned to normal, cough and expectoration practically disappeared, and her weight picked up

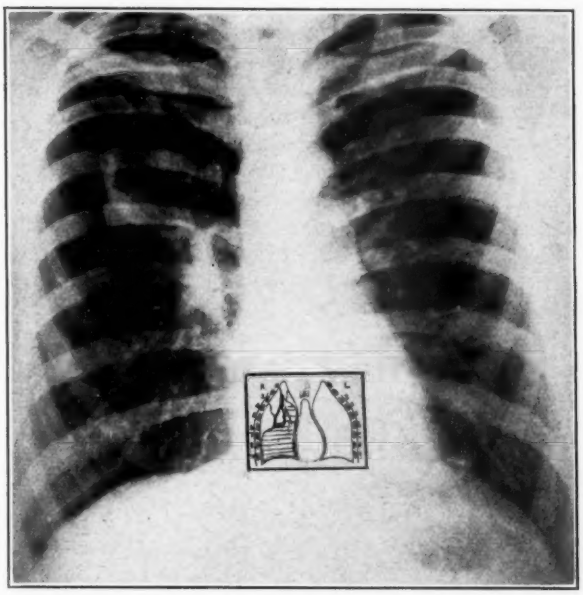


Fig. 5.—Case 2. Shortly after artificial pneumothorax was initiated on the right side. The large cavity can be made out very easily. The shaded area in the diagram represents the uncollapsed part of the lung surrounded by air.

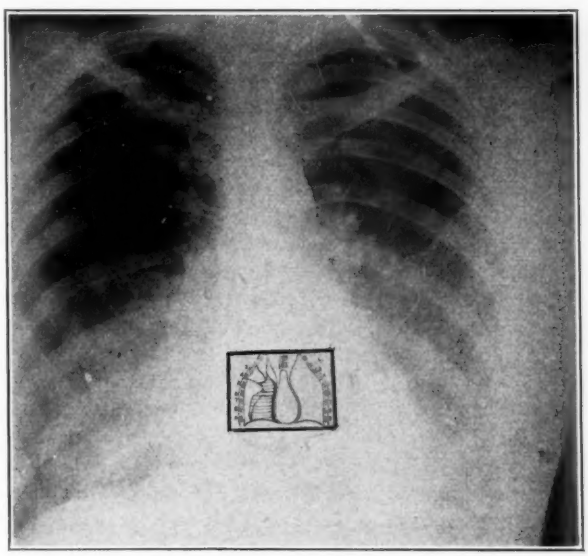


Fig. 6.—Case 2. Complete collapse of the diseased right upper lobe. The cavity is no longer visible, and most of the disease has undergone resolution. The shaded area in the diagram represents uncollapsed lung, surrounded by air. This film was taken September 12, 1931, three months after the patient gave birth to a healthy, female baby, and twenty-seven months after pneumothorax treatment was instituted.

rapidly. On November 17, 1929, the patient was sufficiently recovered to leave the sanatorium and continue with her pneumothorax refills. Nine months later she again became pregnant, but this time insisted on going through with it as she was very anxious for a child. On June 15, 1931, she gave birth to a full-term, healthy, baby girl, weighing eight pounds, three ounces. There was nothing of moment during the entire period of gestation. The patient remained in the hospital the usual two weeks, followed by a period of convalescence at home. Within three months after giving birth she resumed full household responsibilities and has remained in perfect health to date. There was nothing unusual in the management of the tuberculosis problem. Artificial pneumothorax was administered every ten days with an additional refill two days after the delivery in order to ensure reenforced rest to the diseased lung. The treatment is still continued—thirty-three months after the initial refill, and a complete recovery is anticipated.

2104 Pine Street.

A TEST FOR RUPTURED BAG OF WATERS

M. Melvyn Berlind, M.D., C.M., Brooklyn, N. Y.

(Associate Obstetrician, Unity Hospital)

THE importance of knowing whether the bag of waters is ruptured is often of very great moment, especially in a contemplated cesarean section. The diagnosis however is not always a simple matter. The test was tried in 50 consecutive labor cases, in my hospital service, and it proved to be correct, by the subsequent course of the labor, in every case. The method is based on the difference of the P_H of the vaginal and cervical secretions and that of the amniotic fluid. The vagina and cervix during pregnancy have an acid reaction, while the amniotic fluid is faintly alkaline or neutral. Thus by using the indicator brom-thymol-blue (dibrom-thymol-sulphone-phthalein), having a P_H range of 6.0 to 7.6, in the vagina, one can determine the acidity or alkalinity (or neutrality)—an intact or ruptured bag, respectively. In an acid medium the indicator remains an orange color, but in an alkaline or neutral medium it turns green. Thus the green color indicates a ruptured bag of waters, while persistence of the orange an intact bag.

The technic of the test is as follows. White filter paper is cut into strips approximately 1 by 4 cm. These are dipped in a solution of 0.2 per cent brom-thymol-blue, using absolute alcohol as the solvent, and then wrapped in one to two layers of gauze. The ends of the gauze are tied leaving the thread on either end about 10 cm. They are then sterilized by dry heat, and can be kept in a sterile metal container in the labor room. To insert the indicator, an assistant or nurse separates the labia widely, the threads are held in the left hand and with a sterile forceps the gauze-covered indicator is placed in the vagina. Care is to be taken to avoid the anterior part of the vagina and the labia, due to possible contamination by the urine. The indicator is removed by the threads after a minute's stay in the vagina. A change to green color, be it ever so small on the paper, is indicative of a ruptured bag of waters. The orange color remaining speaks for an intact bag.

The author wishes to take this opportunity of thanking Dr. Miklos Temesvary, of the Alice Weiss Kurhaus, for encouragement and interest in the working out of this test during the author's stay in Budapest.

125 Eastern Parkway.

Special Article

THE RÔLE OF FRONTIER AMERICA IN THE DEVELOPMENT OF CESAREAN SECTION

NICHOLSON J. EASTMAN, M.D., BALTIMORE, MD.

(From the Department of Obstetrics, the Johns Hopkins University and Hospital)

WITH the present year the so-called modern era of cesarean section concludes its first half-century; and were one asked in what respect obstetrics has advanced most conspicuously during these five decades, one might fittingly point to the revolutionary changes which have occurred in the indications, the technic, and the prognosis of the cesarean operation. Throughout the greater part of the nineteenth century, cesarean section was the most fatal of surgical procedures. In Great Britain and Ireland, the maternal mortality from the operation had mounted in 1865 to the appalling figure of 85 per cent. In Paris, during the ninety years ending in 1876, not a single successful cesarean section had been performed. The results in Germany, Austria, and Italy were so poor that the newly introduced operation of Porro, which included hysterectomy as well as removal of the child, was superceding the old and almost universally fatal cesarean section; the Porro procedure, it was claimed, saved more than half of the women subjected to it. As late as 1887, Harris noted that cesarean section was actually more successful when performed by the patient herself, or when the abdomen was ripped open by the horn of an infuriated bull. He collected nine such cases from the literature with five recoveries, and contrasted these with twelve cesarean sections performed in New York City during the same period, with only one recovery. In the face of such results, it is not surprising that many obstetricians of the nineteenth century doubted the wisdom of ever resorting to cesarean section, and predicted that the operation would shortly lapse into desuetude.

The turning point in the evolution of cesarean section was clear-cut and decisive. It was the appearance in 1882 of a monograph by Max Sänger, then a twenty-eight-year-old assistant of Credé in the University Clinic at Leipzig. The title of the work, "Der Kaiserschnitt bei Uterusfibromen nebst vergleichender Methodik der Sectio Caesarea und der Porro-Operation," scarcely suggested its real purpose, which was to recommend in cesarean section the routine employment of carefully placed uterine sutures. "The salient consideration in the proposed improvement of the classical cesarean section," he urges, "is without doubt the treatment of the uterine wound"; and through two hundred pages he evolves, amplifies and substantiates this same theme. The history of the uterine suture, the advantage of the buried uterine suture, the best material for sutures—these were a few of the many aspects of the subject which received detailed attention. In particular, Sänger deprecated the growing tendency to abandon the old classical cesarean section in favor of the new Porro procedure, since he believed that careful coaptation of the uterine wound with sutures would obviate all difficulties and permanently establish the superiority of the older operation. Such views were new, for neither in Europe nor in England had uterine sutures been considered necessary. His opinions were at variance, moreover, with the dictates of the most experienced operators of the time—and, let us remind ourselves, Sänger's experience had been limited to but one successful case. His contentions, however, were supported by

such carefully documented evidence, and his facts marshalled in such a logical and convincing manner, that the justice of his claims was apparent. Confirmation of his convictions followed quickly. Within a few years uterine suture was generally recognized as an indispensable part of cesarean section and forthwith the modern operation came into being.

The long neglect of so simple an expedient as uterine suture in cesarean section was not the result of oversight but was due to a deep-rooted belief that sutures in the uterus were superfluous as well as harmful. In 1770, Andre Levret, the foremost obstetrician of eighteenth century Paris, had taught that uterine sutures in cesarean section "were not only prejudicial but were absolutely useless because of the prodigious contractions which the uterine muscle undergoes following delivery." This view that sutures would cut through the uterine muscle and thus defeat their

MAX SÄNGER
1853-1903

own end became widespread and was reflected a hundred years later in the unique work of the Italian surgeon, Silvestri, who sought to obviate this untoward result by employing elastic suture material. In 1874 he and his assistant, Veyer, reported two cases of cesarean section in which rubber bands were used for suturing the uterus. Another compelling argument against the use of uterine sutures was the copious suppuration which followed the suturing of abdominal wounds, a fact which naturally deterred surgeons from hazarding similar procedures in the uterus. In the main textbooks of the period, uterine suture was rarely mentioned, and, if so, but incidentally. Thus, Blundell, in his "Principles and Practice of Obstetric Medicine," published in 1840, dismissed the subject with the remark that "sutures to the uterus have not hitherto been in general employ." Similarly, Caseau, in his "Traité théorique et practique de l'art des accouchements," which was enjoying wide popularity even as late as Sänger's time, commented briefly that "the uterine wound needs no treatment other than to keep it clean."

In other words, throughout the greater part of the nineteenth century, the uterine suture in cesarean section had been in general disrepute. It is true that, in a few isolated cases, it had been used both in Europe and in England, but these instances were not at all illustrative of Sänger's conception, for in them sutures had been employed usually to stop bleeding rather than to unite the wound; as Sänger points out, they were really ligatures. Thus, in the earliest recorded case of cesarean section in which uterine sutures were used, that of Lebas of Mouilleron, reported in 1769, three sutures were inserted, but avowedly for the sole purpose of controlling dangerous hemorrhage. Even this use of uterine suture, however, was so rare that Hasse, in 1856, could find in the literature only six cases in which uterine suture had been employed; and in general it seems clear that at the time Sänger's monograph appeared, neither Europe nor England had had any appreciable experience with this procedure. If, now, in conjunction with this fact, it is also recalled that Sänger's own experience with the uterine suture in cesarean section had been limited to one case, the question arises: whence came Sänger's idea? What were the sources of that carefully documented evidence in favor of the uterine suture? Who were his forerunners? The answer to this question Sänger, himself, states frankly and without reserve. As we have seen, his predecessors were certainly not his colleagues in the sophisticated medical centers of Europe, but were—oddly enough—certain pioneer surgeons working in the outposts of the American frontier. And, without wishing to detract in the slightest from the greater credit due to Sänger, it is the purpose of this article to recall the almost forgotten contributions of these Americans to cesarean section.

The rôle of nineteenth century America in the development of cesarean section was two-fold. It comprised, in the first place, the introduction and the perfection of the silver wire uterine suture, which, as Sänger later pointed out, constituted a turning point in the evolution of the operation; it consisted, secondly, in demonstrating the importance of that axiom of modern obstetrics, namely, cesarean section to be safe, must be done early in labor.

The conception and development of the silver wire suture in cesarean section was wholly an American achievement. In December, 1852, Frank E. Polin, a well known surgeon of Springfield, Kentucky, was consulted in the case of a certain Mary Brown, who had become exhausted from forty hours of labor, the dystocia being due apparently to a hydrocephalic child. Polin performed a cesarean section and closed the uterine incision with silver wire sutures; the patient survived, later bore two infants spontaneously, and was still in good health thirty years later. The details of the operation are scantily reported, and just what prompted Polin to employ sutures in the uterus, and particularly silver wire sutures, is not clear. It is significant, however, that in the January preceding Polin's operation, there appeared the celebrated paper of J. Marion Sims on the use of silver wire sutures in vesicovaginal fistula, and, although Sims did not mention the use of silver wire in cesarean section, it appears that his general idea bore fruit at the hands of the Kentucky surgeon. Polin did not record his case in the literature so that during the ensuing decade and a half, his experience was apparently forgotten. Between the years 1867 and 1880, however, uterine sutures were employed in sixteen cesarean operations in the United States, and in nine instances, at least, the material used was silver wire.

These early American surgeons were correct in believing that the silver wire suture offered them certain peculiar advantages in cesarean section. In the first place it did not require removal. As Sims himself had demonstrated in various abdominal operations, silver wire could be left in the tissues indefinitely as an innocuous buried suture with "no inflammation, no suppuration, no cutting out of sutures, no gaping or retraction of flaps, and therefore no necessity for disturbing

TABLE I. TABLE SHOWING THE EARLY AMERICAN CASES OF CESAREAN SECTION IN WHICH UTERINE SUTURES WERE EMPLOYED
(Translated from Sänger)

CASE NO.	DATE	OPERATOR	AGE AND RACE	INDICATION FOR OPERATION	LENGTH OF LABOR, CONDITION OF PATIENT	KIND AND NUMBER OF SUTURES	OUTCOME MOTHER	OUTCOME CHILD
1	1852	Frank E. Polin	36 White	Hydrocephalus	40 hours. Exhausted	Silver wire sutures	Lived	Lived
2	1867	T. Beers-Townsend	16 Black	Contracted Pelvis	62 hours	3 Hemp sutures. Also 5 ligatures	Lived	Lived
3	1867	D'Aquin and Brickell	23 Creole	Stricture of Cervix and Vagina	10 days. Restless. Pulse 144	6 silver wire sutures	Lived	Died
4	1869	Sager	35 White	Contracted Pelvis (Dwarf)	9 hours. Sick. Has always used crutches	4 silver wire sutures	Died	Lived
5	1870	Pahul de Marmon & Rodenstein	40 White	Contracted Pelvis	44 hours. Exhausted	1 uterine suture	Died	Lived
6	1870	T. A. Foster	40 White	Eclampsia	2 weeks (?). Having convulsions	10 silk sutures	Died	Lived
7	1871	J. U. L. Quackenbush	30 White	Contracted Pelvis (Dwarf)	3 days. Exhausted	2 silver wire sutures	Died	Died
8	1872	E. C. Griffin	37 White	Fibromyomata	No definite pains but exhausted	1 silk suture	Died	Died
9	1874	T. Gaillard Thomas	30 White	Fibromyomata uteri	Few hours in labor. Attempts at version and craniotomy	Silver sutures	Died	Died
10	1875	Jones & Kline	35 White	Sacral exostosis (Dwarf)	38 hours. Exhausted	1 silk suture	Lived	Lived
11	1875	S. S. Lungren	29 White	Contracted Pelvis	Few hours. Membranes intact	5 silver wire sutures	Lived	Lived
12	1876	O. B. Barber	17 White	Contracted Pelvis (Dwarf)	Early operation	3 silver wire sutures	Died	Lived
13	1877	E. W. Jenks	24 White	Contracted Pelvis Shoulder presentation	7 days. Exhausted	4 silver wire sutures	Lived	Died
14	1877	G. E. Walton	19 White	Contracted Pelvis	Long labor. Already sick; abscess in flank; cough; diarrhea. Attempt at forceps	1 silver wire suture	Died	Lived
15	1878	R. G. Curtin	20 Black	Contracted pelvis (Dwarf)	24 hours. Membranes intact	7 carbolized catgut sutures	Died	Lived
16	1880	S. S. Lungren	34 White	Patient same as in Case No. 11	Contracted pelvis. Previous cesarean section	3 silver wire sutures 9 horse-hair sutures	Lived	Lived
17	1880	M. Baker	34 White	Fibromyomata uteri	60 hours	4 silk sutures	Lived	Lived

the dressing till all is firmly united and permanently well.'' This Utopian picture of wound healing was in welcome contrast to the prolonged ordeal of suppuration and sloughing which in those days followed the use of silk, linen and hemp. Particularly in cesarean section, in those few early cases in which uterine sutures had been employed, the irritation and suppuration caused by nonmetallic sutures were so intense that the early removal of the stitches was thought imperative. To this end various expedients had to be devised. Sometimes the ends of the sutures were left long and were allowed to extrude from one end of the abdominal wound; more frequently the lower angle of the abdominal incision was intentionally left open so that the uterine sutures might later be inspected and fished out by sight; some authors even advised that the ends of the sutures be brought out through the vagina and subsequently withdrawn through that outlet. This difficulty in regaining the uterine sutures was, indeed, one of the chief obstacles to their general use. Furthermore, the prevalent practice of removing the uterine sutures on the third or fourth day postpartum prevented their serving any real purpose in effecting permanent coaptation of the uterine edges, and it is not surprising that subsequent autopsy studies on such cases revealed conditions identical with those in which no sutures at all had been employed. In patients who died before removal of the silk or linen sutures, it was commonly observed either that the stitches had cut through the tissues or that the knots had slipped, and in either event the sutures were found dangling loose in the suppurating wound. But all these difficulties, which had seemed so inseparably associated with the insertion of nonmetallic material into the uterus, promised to vanish with the advent of silver wire.

The pertinent facts concerning the seventeen American operations in which uterine sutures were used, are listed in the accompanying table. As is noted in the legend, the table is a translation of one occurring in Sänger's monograph. That Sänger saw fit to collect and tabulate these cases in such detail and that he gave them such prominence in his study, is clear enough evidence of the important rôle they played in the evolution of his hypothesis. It may also be noted that no more convincing proof of Sänger's wholehearted fairness and generosity could be desired than this enthusiastic tribute to his American predecessors. The maternal mortality among the sixteen cases in which the suture material was specified, was 50 per cent, a figure decidedly better than that reported in England for cesarean section and slightly lower than that recorded by the most experienced surgeons on the Continent. Most of these patients had been in labor for days; all of them had been subjected to repeated and lengthy vaginal examinations and in many instances, vain attempts had been made to deliver the women by forceps or craniotomy before the cesarean operation was undertaken. In view of the desperate condition of the patients, indeed, it seems doubtful whether classical cesarean section today would offer such a group a much better outlook. Sänger, however, was interested not so much in studying the gross mortality rate as in the correlation between the maternal outcome and the number and kind of uterine sutures which had been employed; and on the basis of the American statistics he was able to show that the prognosis in cesarean section improved in proportion to the number of uterine sutures used, particularly in those cases treated with silver wire.

It is true that in some of the earlier cases in the group, uterine sutures were employed primarily for hemostasis, but even in these cases, it soon became evident to the operators that the sutures also fostered better wound healing, prevented the escape of lochial fluids into the peritoneal cavity and decreased the likelihood of puerperal peritonitis. Thus, in the earliest of the American cases to be recorded, that reported by Brickell in 1869, the several advantages of the uterine suture are clearly set forth:

"A most important observation was that of the failure of the uterus to contract fully on its own cavity after the ovum was removed. Indeed, the organ had to be freely manipulated to make it contract even moderately. Not only did the blood continue to flow freely from the large wound inflicted, but one side of the flaccid organ absolutely fell in, and had to be lifted up to pass the sutures. . . . .

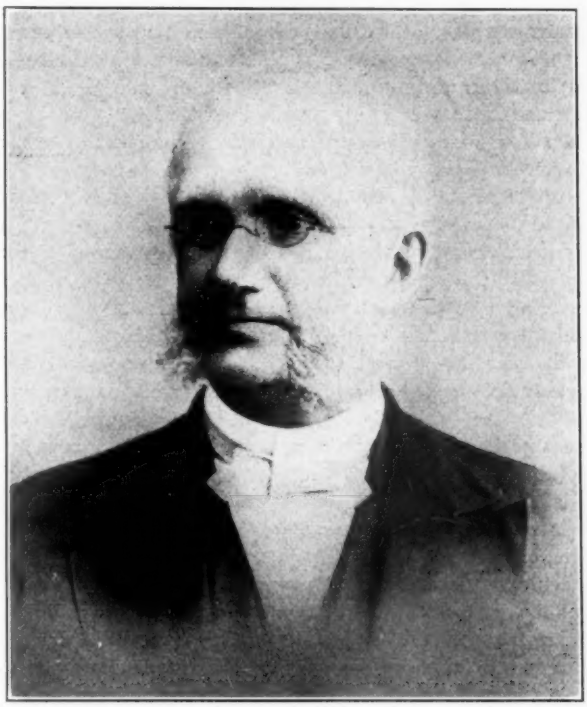
"The remedy for this hemorrhagic condition is, so far as I am aware, novel. With the exigency before us, there could not be a doubt in my mind as to the remedy, and it is seen that not only was the hemorrhage promptly arrested by close adaptation of the cut surfaces of the uterus but the collapsion of the organ was in this way relieved, and the wires have up to this moment proved wholly innocuous. I find in this part of the operation the most interesting point of all. I have long been of the opinion that in all probability the majority of deaths from cesarean section were the result of bleeding from the uterine walls into the cavity of the abdomen—the bleeding itself depressing the woman, and the effused blood lighting up peritonitis. Moreover, I have thought that concomitant with this bleeding was the gaping condition of the wound, the consequent absence of healing by first intention, and the strong invitation to metritis and septicemia. I have often resolved in my own mind to sew up the uterus in case I should be called on to operate, no matter how well it might contract at the time of operation; and on the ground that even the most vigorous uterus, after a normal delivery, is liable to expand and bleed, and in case of the section being made and our sewing up the abdomen over a womb we see to be well contracted, we cannot say that such secondary expansion will not occur; indeed, I contend that we have the right to expect the shock of operation to produce such expansion, and if the organ be not secured by sutures the result must ever be disastrous. I am satisfied that it may be theoretically and practically asserted true surgery to apply the metallic suture to the uterus in all such cases. The innocuous nature of the metallic suture is every day proved in surgery, and there can be no reason for apprehending the danger from its application in every case of cesarean section."

To other American surgeons, the study of the uterine wound, when examined possibly years later at autopsy or at a subsequent operation, afforded further evidence of the value of the uterine suture. Thus, in 1880, S. S. Lungren, a Toledo surgeon, had occasion to perform a cesarean section on a patient who had undergone the same operation five years before. In commenting on the condition of the uterine scar, Lungren observed that "contrary to expectations, no adhesions were found between the uterine and abdominal walls. The uterus was freely movable. . . . . The silver sutures were seen under the peritoneum as bright as when placed there five years previously." The theoretical advantages of the uterine suture were likewise clear to Lungren, as the following passage shows:

". . . . the sutures being introduced partly through the uterus, the peritoneal surfaces are retained in contact until union takes place, and all danger of escape of (lochial) fluids averted. This method of introducing the sutures is the more necessary, for as soon as the incision is made and the contents of the womb extracted, eversion of the lips of the wound takes place to a great degree, the external edges being bevelled off; and as soon as absorption commences below in the interior, the slit would be enlarged, affording ready exit to the fluids. To obviate such results was the aim in the introduction of sutures."

Another zealous advocate of the uterine suture in cesarean section was Charles F. Rodenstein of Westchester, New York, who as early as 1870 stated that "the appli-

cation of uterine sutures after every cesarean section will probably diminish the rate of mortality attending that operation.'' His view was founded on an examination of the records of four hundred cesarean operations performed since the beginning of the nineteenth century. In studying the postmortem findings, he was particularly struck with the frequency of such statements as these: ''the uterus was found open''; ''the edges of the wound gaped''; and ''the uterine incision did not close.'' He reached the inevitable conclusion that the majority of fatalities following cesarean section resulted from the escape of blood and lochia into the peritoneal cavity; but, he advised, ''by closing the wound with sutures, the danger of such unfortunate occurrences may be prevented.''



ROBERT P. HARRIS
1822-1899

The papers of Brickell, Rodenstein, Lungren and others, thus, leave little doubt as to the genuine enthusiasm with which many American surgeons pleaded for the use of the uterine suture in cesarean section. Some years before the appearance of Sänger's work, these men had appreciated the whole rationale of the uterine suture, had shown by their results its many practical advantages and had advocated its employment in every cesarean operation. Yet, it is questionable whether any of their individual reports, which were often brief and appeared for the most part in obscure medical journals, would ever have attracted European consideration if it had not been for the exhaustive studies of Robert P. Harris of Philadelphia, who must be regarded, at least so far as Europe was concerned, as the spokesman for the American surgeons. With unremitting energy he searched the whole country for every case of cesarean section which had been performed, tabulated the circumstances and details of each operation and between the years 1872 and 1881 published

six lengthy statistical surveys covering the whole field of cesarean section in the United States. As Dr. Howard A. Kelly has noted, Harris was the most prominent obstetric statistician this country has ever known, his writings attracting attention both in Europe and in England. Indeed, one of his statistical studies on ectopic gestation involved him in an imbroglio with Lawson Tait, who called him a "library surgeon." Other papers of Harris appeared in German and Italian medical periodicals. The influence which his writings on cesarean section exerted in European circles is amply attested by the fact that in Sänger's monograph his name appears more often than that of any other author, Zweifel, the leading German authority on cesarean section, not excepted. If it be granted then, that Sänger's acquaintance with cesarean section in the United States was derived from Harris' papers, what did the German author learn there concerning the American attitude toward the uterine suture? Did Harris recommend its routine employment? This question is important, since its answer explains Sänger's honest belief that he was the first to advise the routine use of this procedure. Harris did not advocate the insertion of uterine sutures in every cesarean section, but only in certain selected cases. In general, he was inclined to reserve his opinion, and as late as 1878 remarked that "the experience of our country is as yet entirely too limited to determine whether the employment of the uterine suture is, or is not, an improvement in the method of operating. . . . . The fear has been that sutures in the uterus would greatly increase the danger of peritonitis; but the dangers to be encountered by using them are often not to be considered, in view of the greater risks in endeavoring to avoid their employment. In atony or hemorrhage at the time of the operation, there can be no question as to the better safety of the suture." It was thus, with faint praise, that the spokesman for the American surgeons reported his country's experience with the uterine suture in cesarean section.

But upon another important issue in cesarean section, Harris took a much firmer stand and was adamant in his insistence that cesarean section to be safe must be done early in labor. This one unifying theme runs throughout his writings; and whether he deals with "cattle-horn cesarean section" on the plains of the West or with the results of cesarean section in the hospitals of New York City, he invariably finds evidence in support of the "timely operation." This teaching that cesarean section be performed early in labor has since proved to be the watchword to success in the operation, and as it was first announced clearly by American surgeons, it deserves recollection as one of the creditable contributions of this country to obstetrics.

It must be noted, however, that the advisability of early operation had already been suggested, at least, by Thomas Radford of Manchester, England. In 1865, this author analyzed all the recorded cases of cesarean section in Great Britain and Ireland and, after finding that the maternal mortality of the series was 85 per cent, advanced the opinion that better results might be obtained if the operation were performed earlier in labor as a procedure of choice rather than being delayed until it became one of necessity. He cites no figures to substantiate his opinion, however, and summarizes his views in the following two sentences: "Notwithstanding all the preexisting dangers of cesarean cases, several recoveries have taken place. The favorable terminations ought to encourage us to hope, and indeed ought to inspire us with confidence, that if the operations were earlier performed, and on a different class of subjects, it would be attended with infinitely more success." Until the close of the nineteenth century in fact, it was still held that the most favorable time for performing cesarean section was at the end of the first stage of labor, an attitude prompted by the belief that the hemorrhage incident to incising the uterus would be minimized if the uterine muscle was in a very active state of contraction.

To perform cesarean section before the advent of labor was thought to be particularly dangerous and even after Bar of Paris, in 1888, had reported favorable results in cesarean operations done at this time, the practice was still regarded as hazardous. In view of this doctrine, the natural tendency to delay so dangerous an operation until it was clearly imperative met with general approval, and cesarean section remained an operation of last resort.

The first of Harris' papers attacking the evils of delay in cesarean section appeared in 1871, and from the beginning the author pleaded with compelling logic and vigor in behalf of the early operation. Some of the evidence upon which he based his contentions was unique. Thus, he called to mind, in the first place, that the first cesarean section to be performed upon a living woman was said to have been done in 1500 by a Swiss sow-gelder upon his wife, with happy results both for mother and child. The first authentic operation in the British Isles was one performed by a common midwife, Mary Dunally, upon a certain Alice O'Neal of Ireland, in 1739. The outcome was successful, although in the next thirty-seven cesarean sections performed by physicians in Great Britain between 1739 and 1845, only three women survived. The first recorded cesarean section in the United States was performed in 1822 by the patient herself, a fourteen-year-old quadroon servant, who made an "L" shaped incision through the abdominal wall and uterus while lying in a snow bank; she also recovered. Having noted these facts, Harris then extended his observations to more recent years and in studying the conditions in this country found that the mortality from the operation actually seemed to increase in direct proportion to the skill of the surgeon and the excellence of his equipment. For instance, the highest death rate was reported for New York City and State, where among twelve women subjected to cesarean section by surgeons and surgical accoucheurs of considerable eminence, but one mother survived. Some of the best results, on the other hand, came from the prairies of the West, where, as we have already noted, the outcome was often favorable even in cases in which the abdomen had been ripped open by the horn of a bull. Particularly gratifying were the figures reported from the plantations of Louisiana, where the mortality from the operation among the slave women was but twelve and one-half per cent, although in New Orleans three-quarters of the mothers subjected to cesarean section had died. Similarly, in the farm houses of Indiana, Ohio and Kentucky, the operation was frequently successful. From Mexico, Cuba, Jamaica, Martinique and Tortola, came reports of eight cases of cesarean section with seven maternal recoveries. Indeed, it seemed that the farther from civilization the operation was done, the greater the likelihood was of success. The truth of this paradox Harris emphasized even more strikingly by showing that in "the open country" of the United States, the maternal mortality from the operation was but 38 per cent, while in the towns and villages it was 65 per cent and rose still higher in the large cities. What could account for these inconsistencies? Were surgical skill and hospital care of no avail? Of course they were, answered Harris, but they could not offset the dangers caused by delaying the operation; and it was in the cities, Harris showed, that delay was most common, the delay which so often comes from multiplicity of counsel. In the open country, on the other hand, either by accident or by the boldness of ignorance, the operation was performed early in labor while the patients were still in good condition, and hence it was successful. Certainly, in the case of "cattle-horn cesarean section," an accident that usually occurred before labor had even begun, such an interpretation was the only available one. Today, we might be inclined to supplement Harris' explanation with other factors, but in the main his tenets were sound; it was the countryside, the American frontier, which first demonstrated the safety of cesarean section.

Other types of cases were likewise grist for Harris' statistical mill and afforded

additional evidence in favor of the "timely" operation. Thus, in cases of rupture of the uterus during labor, he found that abdominal delivery was a relatively safe procedure. One might think that this operation, performed after rupture of the uterus in order to remove the fetus and its secundines, would turn out to be a more severe and fatal operation than cesarean section, but such was not the case, and, as Harris pointed out, for two reasons. In the first place, where rupture of the uterus occurred, the necessity for a prompt operation was generally recognized both by the accoucheur and the surgeon; and secondly, the subjects of rupture were as a general rule in better condition than those who eventually subjected themselves to cesarean section. Still more convincing were the lessons which Harris drew from another class of patients; namely, those upon whom cesarean sections had been repeated. In such cases, the circumstances which had necessitated the previous operation usually made it clear that a natural labor would be impossible and accordingly cesarean section was decided upon at an early date and carried out either at the onset of labor or shortly after. Here, then, was a group of cases which exemplified *par excellence* the teachings which Harris had advanced, and, as he had predicted, the results were startling. Among nineteen operations performed on nine women, there were only three maternal deaths. By adding to these American statistics those of similar cases from other countries, it was shown by Lungren that a total of one hundred and nineteen operations had been done on forty-eight women with only eight maternal deaths, or in other words, with a maternal mortality of less than seven per cent, which in 1881 was an unheard of figure. So, by utilizing cases of various sorts from many sources, Harris, Lungren, and other American writers made it plain that cesarean section in this country was in general attended by a maternal mortality of about fifty per cent, but that when the operation was performed during the first twenty-four hours of labor, the mortality fell to twenty per cent, while in operations done at the onset of labor, as in repeated cesarean sections, it dropped to a level below ten per cent. It is not surprising, therefore, that Harris was such a fervent champion of the "timely" cesarean operation and that, somewhat before Sänger, he urged its superiority over the Porro procedure in the following words:

> "I do not feel that there is the same demand for a change in the United States, where the old operation has had so large a measure of success, especially when performed in a few hours after the commencement of labor. Let the cesarean operation be one of election and anticipation as the most successful Porro sections have been; let it be performed under carbolic spray; the abdominal cavity thoroughly cleansed from blood and amniotic fluid; the uterine wound, if need be, closed with silver wire; let a drainage tube be introduced, and the parts be dressed according to the methods of Keith and Lister; and we shall expect in this country to save more cases than has been done, in proportion, in any European hospital, under the Porro method."

However, in attempting to evaluate the accomplishments of these nineteenth century Americans, it is important not to lose historical perspective. After all, it was Sänger's study which dealt the final blow to the old cesarean methods. At a time when all of Europe was clamoring for the radical Porro procedure and England was turning to craniotomy, he proved to his colleagues on undeniable grounds the superiority of the conservative cesarean section; he not only advocated the routine use of aseptic uterine sutures, but showed in the minutest detail how to insert them; and by combining the scientific principles of wound coaptation with full Listerian technic, he created at one stroke the modern operation. But, to have furnished the supporting data for Sänger's hypothesis, to have devised and demonstrated the earliest successful type of uterine suture and to have shown for the first time the

immeasurable value of the "timely" operation—these were certainly no mean achievements and may be recalled with pride as contributions of frontier America to cesarean section.

REFERENCES

Brickell: A Successful Case of Caesarean Section, New Orleans J. Med. **21**: 454-466, 1868. *Dibble:* A Successful Case of Caesarean Section, Med. Rec. **3**: 1-2, 1868. *Harris:* The Caesarean Operation in the United States, Am. Jour. Obst. **4**: 409-439, 622-663, 1872. *Harris:* The Operation of Gastro-Hysterotomy (True Caesarean Section), Viewed in the Light of American Experience and Success; With the History and Results of Sewing Up the Uterine Wound; and a Full Tabular Record of the Caesarean Operations Performed in the United States, Many of Them Not Hitherto Reported, Am. Jour. Med. Sc. **75**: 313-342, 1878. *Harris:* Lessons From a Study of the Caesarean Operation in the City and State of New York, and Their Bearing Upon the True Position of Gastroelytrotomy, Am. Jour. Obst. **12**: 82-91, 1879. *Harris:* Special Statistics of the Caesarean Operation in the United States, Showing the Successes and Failures in Each State, Am. Jour. Obst. **14**: 341-361, 1881. *Harris:* Does the Removal of a Foetus by Abdominal Section, After Rupture of the Uterus, Constitute a "Caesarean Section"? Am. Jour. Obst. **14**: 856-865, 1881. *Harris:* Cattle-Horn Lacerations of the Abdomen and Uterus in Pregnant Women, Am. Jour. Obst. **20**: 673-685, 1887. *Jenks:* Report of a Successful Case of Caesarean Section After Seven Days' Labor, With Some Comment Upon the Operation, Am. Jour. Obst. **10**: 606-612, 1877. *Kelly and Burrage:* American Medical Biographies, Baltimore, 1920. *Lungren:* A Case of Caesarean Section Twice Successfully Performed on the Same Patient, With Remarks on the Time, Indications, and Details of the Operation, Am. Jour. Obst. **14**: 78-94, 1881. *Radford:* Observations on the Caesarean Section and on Other Obstetric Operations, Manchester, 1865. *Rodenstein:* On the Introduction of Sutures Into the Uterus After Caesarean Section, Am. Jour. Obst. **3**: 577-582, 1871. *Sager:* Case of Delivery by Caesarean Section, Mich. Univ. Med. Jour. **2**: 385-393, 1871. *Sänger:* Der Kaiserschnitt bei Uterusfibromen nebst Vergleichender Methodik der Sectio Caesarea und der Porro-Operation, Leipzig, 1882. *Sims:* Silver Sutures in Surgery, New York, 1858. *Williams:* A Comparison Between the Caesarean Section and the High Forceps Operation, Am. Jour. Obst. **12**: 23-31, 1879. *Winckel:* Handbuch der Geburtshülfe, Munich, 1906, vol. 3, 669-810.

Walther: The Value of Bisection of the Superior Hypogastric Plexus in the Treatment of Pelvic Neuralgias. Bruxélles-méd. **10**: 29, 1929.

The superior hypogastric plexus innervates essentially the tubes and uterus but it does not supply the ovaries. For this reason section of this plexus leaves intact the sensibility of the ovary. The plexus is composed almost entirely of sensory fibers and its ablation has no effect on the muscular contractibility of the uterus. Walther has practiced section of this plexus on 14 patients. In eleven the complaint was that of severe dysmenorrhea, while in three the pain was persistent and intermenstrual in type. Twelve of the patients were cured or greatly relieved while only in two cases there was no relief. One of these failures was explained on the basis that the pain was ovarian in origin while in the other the uterine pain was relieved but a coccygodynia persisted.

The operation is indicated in cases of metritis or chronic painful salpingitis where medical treatment has failed and where because of the patient's age castration is to be avoided. It is not indicated in pain of ovarian origin.

THEO. W. ADAMS.

American Journal of Obstetrics and Gynecology

GEORGE W. KOSMAK, M.D., EDITOR HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Editorial Comment

THE MODERN CESAREAN OPERATION

A HALF century has passed since Max Sänger published in Leipzig his monograph on the suturing of the uterus after cesarean section. We must regard this as one of the most outstanding contributions to obstetric surgery. It is therefore fitting for the JOURNAL to take note of this anniversary year, by publishing in the present issue a paper by Dr. N. J. Eastman, of Johns Hopkins, in which the interesting fact is brought out that certain pioneer surgeons of America furnished the basis for Sänger's improved operation, as he himself duly acknowledges. And it is to the files of the predecessor of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY that many of these noteworthy contributions to the literature were made. We are pleased therefore to round out this record by giving space to the interesting article of Dr. Eastman in the current issue.

Perhaps the occasion should call forth a word of comment on the acceptance of this obstetric operation, no longer as a procedure solely of necessity, but rather as one of choice. It is a far cry from the days of Sänger, when by mere suture of the incised uterine wall, the dangers of the operation were largely reduced. And yet the element of risk has not been completely eliminated, for we still find a considerable mortality associated with cesarean section as compared with surgical laparotomies in general. Where must we seek the cause? Is it due to lack of skill, of failure to observe proper indications, or have we substituted without proper justification, a procedure purely surgical, for others more essentially obstetric in their underlying requirements? Cesarean section is not difficult of execution by a well trained surgeon, it offers an easy solution of many obstetric problems and its performance is always attended with a certain theatric glamor. But the mortality rate which has accompanied cesarean section even in recent years, except in the best ordered clinics, shows that the operation is not as free from danger as its enthusiastic advocates would lead

us to believe, and that we must continue to seek, as Sänger did, the means to place it on a firmer basis, with due regard to the indications for its performance and the qualifications of the operator. Perhaps the success of such efforts will show a lowered mortality and morbidity rate during the next half century, with consequent greater safety to the mother and that such progress may be recorded with justified pride in a future issue of this JOURNAL, should it survive to commemorate the hundredth anniversary of the Sänger operation.

Society Transactions

AMERICAN GYNECOLOGICAL SOCIETY

FIFTY-SEVENTH ANNUAL MEETING

Quebec, Canada

MAY 30, 31, AND JUNE 1, 1932

(Continued from November issue.)

Anterior Pituitary Lobe and Genital Function, Dr. Bernhard Zondek, Berlin, Germany. (By invitation.) (See page 836 for original article.)

DISCUSSION

DR. ROBERT T. FRANK, NEW YORK CITY.—Recently I have preferred the Friedman modification of the pregnancy test as it can be used with mature animals, namely, rabbits. Isolation of the animals is not important and even if by accident a pregnant animal should be used superovulation is so strikingly superimposed upon the ovary that the test is likewise quite characteristic. The ovary macroscopically shows large blood spots, more readily recognizable than in the original Aschheim-Zondek test. In some 500 cases we have been able to find correct results in 90 per cent within twenty-four to thirty-six hours, meaning that thereby no positive results had been negatived by the clinical history thereafter, but a certain number which I did not count in this percentage have at first proved negative and later, on repetition of the test, showed positive. We were able to recognize three cases of obscure tumors of the lung by the pregnancy test, which was positive, as chorioepitheliomata.

As regards the possibility of two hormones, mentioned by Prof. Zondek, we believe that there is really one hormone only, which produces both the follicle growth and the luteinization, and that this is a quantitative response.

Our attempts to duplicate Zondek's work on tumors I must say was disappointing. We did not study more than 30 cases but the results were so discordant that we stopped this work.

Consideration of a New Viewpoint on the Etiology of Renal Tuberculosis in Women, Dr. Guy L. Hunner, Baltimore, Md. (See page 706, November issue.)

DISCUSSION

DR. JAMES W. DUNCAN, MONTREAL, CANADA.—The technic employed by the essayist is of course different from that which is used by the majority of us. Dr. Hunner uses a much larger catheter. One wonders sometimes if the "hang," sensed by the speaker, may not at times be due to peristalsis in the musculature of the ureter excited by the irritation of the catheter.

DR. JOHN A. SAMPSON, ALBANY, N. Y.—I would like to ask whether Dr. Hunner uses the indwelling catheter for the purpose of maintaining drainage? If so, how long does he let it stay in and with what results?

DR. HUNNER (closing).—Dr. Rushmore spoke of the necessity for tests of function. That is one of the evidences that we are dealing with obstruction, the great in-

crease in phenolsulphonephthalein output after we give the patient better kidney drainage. I appreciate fully the skeptical attitude that most men have had toward each of my tradition-breaking suggestions. There was great opposition when I first proposed the drainage methods for hydronephrosis and for pyelitis, and later for patients suffering with stone, and still later for the cases of essential hematuria. I think men are coming to appreciate more and more the great value of drainage for all of these conditions, and I believe that we are going to learn to use these drainage methods in our selected cases of tuberculosis of the kidneys.

We do not use an indwelling catheter in these cases but simply depend upon repeated dilatation of the stricture at ten day intervals. The indwelling catheter is most valuable in some critical cases of pyelitis of pregnancy, and in some acute surgical conditions when we are trying to tide the patient over for a favorable time to operate. I have left an indwelling catheter for as long as three weeks, irrigating the kidney twice daily with 1 to 5000 silver nitrate solution.

Chemical Changes in the Parturient's Blood, Dr. H. Siedentopf, Leipzig, Germany. (By invitation.) (See page 696, November issue.)

DISCUSSION

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—I believe the work of Dr. Siedentopf may explain some of the cases of shock that take place after delivery.

In normal pregnancy we used to speak of a mild acidosis. This has been shown by Ward and Peters to be due to an alkali deficit, the sodium ion being most diminished. During a long labor, the patient receives little or no nourishment. Organic acids, both ketone bodies and lactic acid can accumulate, and it is reasonable to assume that a condition of acidosis could occur just at the time of delivery. The remarkable thing in Dr. Siedentopf's figures, is the transitory nature of this acidosis, the return to normal after labor being very prompt.

The Influence of Sex Hormones on the Reticuloendothelial Cells of the Uterus, Dr. C. Frederick Fluhmann, San Francisco, Calif. (By Invitation.) (See page 654, November issue.)

DISCUSSION

DR. JAMES R. GOODALL, MONTREAL, CANADA.—It is a very singular thing that oftentimes for years a course of treatment is adopted without knowing the real cause of the beneficent results which follow. Reticuloendothelial cells, that is a large name for a small cell, and we speak of them as macrophages or macroblasts, are not restricted to the uterus alone. They can be called forth in any part of the body. If an irritant is introduced into the abdomen or the blood of the patient, within twenty-four hours the reticuloendothelial cells are present in very large numbers. It is generally conceded that these cells are the lining cells in the lymphatic spaces, which under irritation, adopt a function which otherwise they do not possess. They become exceedingly large, wandering cells. The consensus of opinion is that they have very little to do with the destruction of microbes but their chief usefulness lies in the absorption of destroyed material. They are scavengers and I have advanced recently the idea, why ectopic gestation cases do so remarkably well after operation. In spite of their depletion, it is extremely seldom that you see any peritonitis after these operations, due to the fact that the blood in the abdomen has evoked these cells to activity.

There is another interesting factor: that if you examine the lymphatic spaces of any part of the body after a blood transfusion you will find, depending upon whether the matching had been perfect or not, but more especially in those cases where the matching has not been perfect, a widespread calling out of these cells and I think that in that

reaction lies one of the great virtues of blood transfusion against infection. It is very interesting to know that the hormones evoke this reaction. It has been a question in my mind why during pregnancy these cells should be so active in the uterus, but we find them also in the broad ligaments.

DR. EMIL NOVAK, BALTIMORE, MD.—The work of Dr. Fluhmann may indicate the possible rôle of the hormones in the vascular phenomena of menstruation, concerning which so little is as yet known. In our own studies of the human endometrium, we have been struck with the massive infiltration of leucocytes and large mononuclear wandering cells into the endometrium just before menstruation. This infiltration is apparently analogous to that which Dr. Fluhmann has observed in his experimental work. In the first half of the cycle the endometrium is quite clear of infiltration cells, but just before the beginning of menstrual desquamation the infiltration is so intense that, if one is not familiar with its normality, the picture would suggest a marked inflammatory process.

Presumably this phenomena is due to the cumulative effect of progestin, but its significance is not clear. When it is better understood, and when we know more about the effects of the sex hormones upon the blood vessels of the endometrium, we shall have taken a great step toward a clearer understanding not only of normal menstruation, but of such menstrual disorders as functional bleeding. I have always felt that the latter is not to be explained on the basis of simple tissue loss as a result of localized areas of thrombosis and necrosis, according to Schroeder's ideas, but that there must be some fundamental change in the permeability of the blood vessels themselves in order to explain the extreme hemorrhage so often seen in these cases.

DR. FLUHMANN (closing).—I should like to emphasize the point that it cannot be correctly stated that the hormones directly stimulate the reticuloendothelial system. On the basis of these experiments the only thing we can say is that the appearance of these cells is apparently an indirect effect. The hormones stimulate tissue growth and a local increase of blood vessels and as a result the tissues acquire the power of responding to trauma very much more readily with macrophages.

Reconstruction of the Oviducts: An Improved Technic With Report of Cases, Drs. Frederick C. Holden and Francis W. Sovak, New York City. (Paper read by Dr. Sovak.) (See page 684, November issue.)

DISCUSSION

DR. JAMES E. KING, BUFFALO, N. Y.—The problem of absolute sterility belongs clearly within the realm of surgery. The attitude of any surgeon toward such operations will depend somewhat upon what he may consider to be the criterion of success. Since the Rubin insufflation one's success may be judged by two criteria: first, the permanent patency of the tubes; and, secondly, the number of pregnancies which result from any procedure. In the past, results were judged entirely by the number of pregnancies that followed surgery and as the percentage of successes measured in this way was extremely low, it is not surprising that many of us have been rather cold toward tubal reconstruction. The Rubin insufflation, however, will give, I am sure, a new impetus to this type of surgery, and we now may have the two criteria of success, the persistent patency and the number of pregnancies which follow in a given series.

Dr. Sovak and Dr. Holden have taken as their own yardstick of success the permanent patency following operation. In this they were clearly justified because their operations were done in cases which were indicated for other reasons and they very frankly state that the procedures were done in their series for the purpose of developing the technic of the new procedure. The discussion therefore upon this paper focuses upon the procedures themselves. I have had no experience with the Bonney cuff operation, for I have always chosen in those cases of distal occlusion to split the end of the tube

and evert the membrane. It seems to me that, theoretically at least, that offers a little better chance because of the larger ostium which it affords. It would have been very interesting to me if they had commented upon the condition of the ovaries in their cases for certainly ovaries which require dissection to free their adhesions are in a condition which would make them likely to have new adhesions form with any new peritoneal contacts. Such ovaries in themselves might prevent normal follicle rupture.

The interest centers, of course, around this new procedure of implantation. I think very few of us have been enthusiastic about implantations of the tubes as has been formerly proposed, especially those ectopic implantations where the tube was placed somewhere outside of its normal position. The most important step, I should feel, in the implantation operation is the reaming out of the interstitial portion of the tube. Certainly this gives a wide lumen or opening for the implanted tube and such contractions as might occur as a result of the operative procedure or by contractions of the uterine muscle would not be sufficient to close or constrict the tube.

In one case in which both procedures were done, implantation and circumcision of the tube, and which was followed by pregnancy, I should call a real achievement. In my experience I have found that the cases of nodosa salpingitis are almost always associated with a distal occlusion and that would make it necessary, it seems to me, in many cases to do both of these procedures.

The value of insufflation in sterility operations is important in accomplishing three things: the first in diagnosis; the second in maintaining patency; and the third in determining the future condition of the tubes. I am personally a convert to Dr. Sampson's theory of endometrial implantation and I am just wondering whether in insufflation so early after operation there is not a possibility, theoretically at least, of pushing through endometrial cells that may find a site for implantation.

If success is based alone upon the number of pregnancies I think we may be privileged to take a stand as to what success means. Personally I feel that any procedure that will reclaim a very small proportion of a considerable number of these unfortunate women who are despairing and hopeless in their barreness, justifies surgery. If these gentlemen themselves had taken as the standard for their success the number of pregnancies that followed in their series they might have done so with great credit to themselves. I think they have shown an unusual number of successes.

DR. EDWARD H. RICHARDSON, BALTIMORE, MD.—It was inevitable, of course, following the advent and development of tubal insufflation and hysterosalpingography that attention should sooner or later become riveted upon devising practical methods for restoring function to occluded tubes. Unfortunately I cannot add anything to this report from personal experience because I have never done a tubal implantation. However, a brief summary of the literature may be worth while, since Dr. Sovak did not have time to present one.

It is noteworthy that this operation was first done by an American surgeon, Thomas J. Watkins, who in 1897 first performed a tubal implantation in a woman from whom the other tube had previously been removed. The operation was followed by pregnancy which terminated in abortion. Another American gynecologist, Dr. T. S. Cullen, in October, 1919, performed the second operation of this type and achieved the first successful result on record. He implanted the outer portion of a patient's only tube after resection of the cornual end. Pregnancy occurred ten months later and was terminated by abortion. A second pregnancy occurred, however, which went to term and produced a normal child in June, 1922.

In addition to this report of Dr. Sovak's, I have collected from the recent literature reports of 58 tubal implantations. It is interesting that no American gynecologist is included in this group since the original reports of Dr. Watkins and Dr. Cullen. This contribution, therefore, is particularly timely and creditable to its authors. The ultimate result in most of these 58 cases is not ascertainable from the reports. However,

7 full-term pregnancies, 1 premature birth, 1 abortion and 1 tubal pregnancy, are known to have resulted. Undoubtedly this percentage of success is too high because many failures have doubtless never been reported. It is significant that no report has been made of a normal pregnancy following implantation where a salpingostomy was done at the same time. Heuck reports one tubal pregnancy which occurred under these conditions, and some authors very strongly condemn implantation where the other end of the tube is occluded, believing that there are other factors involved besides mere tubal patency. They interpret hydrosalpinx as indicative of permanent damage both to the tubal musculature, causing impaired peristalsis, and also to the cilia of the epithelium both of which results seriously interfere with the progress of the ovum through the tube and, therefore, predispose to ectopic pregnancy.

The indications for the operation are (1) occlusion of the uterine end of the tube by removable tumors; (2) tubal pregnancy in the uterine end; (3) nodular salpingitis; (4) congenital occlusion of the uterine end; (5) accidental section of the tube during some other operation; and (6) reconstruction following previous sterilization by ligation and division of the tube.

The technic of the operation as described in the literature is interesting in comparison with the method we have heard described today. The weight of evidence favors the cornua as the choice location. Preference varies, however, between the linear, the sagittal incision, and a trephine or reaming operation. Both Kiparsky and Sellheim have devised special trephine instruments which differ in some respects from this one of Dr. Sovak's. In all cases followed by pregnancy either a sagittal section or a cuneiform resection was done. Success has followed both splitting and nonsplitting of the implanted tubal end, but the majority of authors recommend splitting.

Just a word in closing about salpingostomy without implantation. A recent tabulation by Schmitz of Chicago of 371 cases reported by 13 authors showed 31 subsequent pregnancies, 8.36 per cent success. While a little apart from the operation we are considering today, this is a closely related subject. Naturally, salpingostomy is worthless unless patency of the tubes is at the same time established by means of retrograde insufflation.

DR. HARRY DORMAN, BAYREUTH, SYRIA.—In the country where I practice, in the Near East, a large majority of the gynecologic practice is due to sterility.

The first case that I opened at the fimbriated end conceived within six months and has since had three children ⁴hough she had been married seven years before without having a child. She had had an abortion followed by occlusion of the tube. I have done altogether probably ten or twelve implantation operations, following very much the method described by Dr. Sovak, except that I did not have his reaming instrument. In the first case of implantation I had the beginner's luck and the woman had two children.

There is also the question as to whether the thickening of the tubes has interferred with peristalsis and whether the change in the mucous membrane also interferes with the passage of the ovum and conception. One thing I have noted is that the occlusion at the fimbriated end and occlusion at the isthmus are not merely the question of a different operation, but it also involves the change in the mucous membrane. The tube may be closed at the fimbriated end and the mucous membrane of the tube be fairly intact, but when you have an occlusion at the inner third it means a more serious lesion of the mucous membrane of the tube. When I take out a section of the tube from the isthmus I send it to the laboratory and ask them to show me the stricture.

DR. SOVAK, NEW YORK CITY (closing).—A woman has a peculiar psychologic make-up and wishes to be as nearly normal at all times as the other woman and will submit to any type of operative procedure to become normal. A woman with bilaterally diseased tubes, knowing that she has them, is also sick mentally, sometimes bordering on the psychopathic state, and even though you may not have pregnancy follow in all

cases, there is relief of the mental state and I think that should be considered in attempting reconstruction work.

In answer to Dr. King regarding the condition of the ovary, adhesions, etc., I think the heat treatment and suspension of the ovary overcome the congestion and relieve the inflammatory condition.

The early insufflation following operation is a fair criticism. We attempted to see how early we could do an insufflation test and, although we have had no morbidity following the attempt, we are not doing it as early as formerly.

In reply to Dr. Richardson and Dr. Dorman in reference to the damaged tube, we all know that a patient having had a virulent gonorrheal infection or a postabortal infection does become pregnant and there is no reason why a reconstructed damaged tube should not help in the production of pregnancy.

The Relation of Placental Infarcts to Eclamptic Toxemia, A Clinical, Pathologic and Experimental Study, Dr. R. A. Bartholomew, Atlanta, Ga. (By invitation.) (See page 797.)

DISCUSSION

DR. A. H. MORSE, NEW HAVEN, CONN.—Dr. Bartholomew's paper may be discussed from two angles. (1) The frequency of placental infarcts in the toxemias of pregnancy and (2) the effect of the injection into experimental animals of extracts of autolyzed placental tissue. Young has emphasized the possible relation of infarcts of the placenta to eclampsia. Young's theory holds that the presence of infarcts, even those which are ultramicroscopic in size, accounts for the clinical symptoms of toxemia. As is well known, the degenerative changes resulting from infarction form the most common abnormality of the placenta. However, from a gross and microscopic examination of some thousands of routine specimens I have never been convinced that the degree of infarction played a particular rôle in the causation of eclampsia. This viewpoint seems to be borne out by a roentgenographic study of placentae made in our clinic by Thoms. Thoms, after sectioning the injected and hardened organs measured the degree of infarction. Of three patients with definite toxic symptoms, the placenta in one case showed an infarction of 15 per cent; while in the other two no measurable lesion was present. On the other hand, ten patients who presented no symptoms of toxemia expelled placentae in which the percentage of infarction varied from 2 to 24. In any case, as Essen-Moller puts it, we still face the problem that all pregnant women carry placentae but that all do not have eclampsia. The fact that primiparae are more commonly afflicted than multiparae, might be explained by the fact that the latter gradually acquire an immunity. But here again we must explain why some primiparae escape.

The theory regarding the toxicity of broken-down cellular tissue recalls the deportation theory of Veit, the theory of Rosenau and Anderson, that eclampsia might represent an anaphylactic reaction and finally that of several German investigators who suggested that eclampsia depended upon the release into the circulation of placental endotoxines. Veit injected rabbits intraperitoneally with emulsions of placenta. This was followed by the appearance of albuminuria and sometimes by death. However, a similar stage is set when a tubal pregnancy ruptures and expels the ovum into the peritoneal cavity or when the placenta of a secondary abdominal pregnancy is left in situ at laparotomy. Yet in neither instance do symptoms of toxemia necessarily arise.

Murray and Johnstone who repeated Rosenau's work showed that while shock might be induced by the injection of extracts of autolyzed placenta, no similar reaction was induced when unautolyzed emulsions were employed. On the other hand they could reproduce toxic symptoms with extracts made from autolyzed liver.

I would therefore raise the question, whether the reaction on the part of the experimental animals would have been the same had the extracts of placenta been unautolyzed,

and also whether a reaction similar to the one reported by Dr. Bartholomew would not have been induced by the injection of an autolyzed extract of some other protein.

In considering the possible relation of abnormal placenta functions to the toxemias, we should not lose sight of the fact that during pregnancy there is a notable increase in the production of hormones. The human placenta contains folliculin and at least one other hormone which simulated that of the hypophysis. As Zondek has pointed out, this raises the question whether the placenta takes part in the production of hormones or whether it is only a resorption area for hormones produced in the hypophysis and in the ovary. In either case it is pertinent to ask whether a disturbance of this function by itself or associated with aberrations of other endocrine glands may not play a rôle in the toxemic manifestations in question.

Finally it is entirely logical to assume that abnormal placental functions play a part in the causation of the toxemias but fortunately it is exceedingly difficult to prove.

DR. JOHN R. FRASER, MONTREAL, CANADA.—It would seem that the most outstanding change brought forth in this work is the extensive degeneration apparently present in toxemia. However, if one undertakes an age period study of the changes in the placenta from the time of its development through to maturity, it is apparent even in the early stages of the placenta that degeneration is a physiologic change to some extent. We are familiar with the epithelial changes which appear after the fifth or sixth month. Then one is very much struck in the last three months of pregnancy with the frequency by which the degenerative phenomena appear. It would seem almost that this degeneration is a normal physiologic change in many placentas.

There are some very interesting changes in the placenta which one may find from time to time. For instance, in the chronic nephritic very marked degenerative changes are usually present. Then there is a small proportion of cases where the baby dies shortly before term in which an adequate explanation is not forthcoming, in which one may be able to show a rather diffuse degeneration which might be the cause of the unaccountable death.

Then one finds in some cases very extensive degeneration and not much evidence of toxemia. I have personally always looked upon the extensive changes which one sees in a chronic nephritis and in some forms of toxemia as perhaps being aggravated by the toxemia. That is to say, the degeneration which may be present to some extent is increased by the toxemia and I would rather perhaps put that interpretation upon it than, as some people do, for the cause of the toxemia.

The life history of the placenta is 280 days. Senility appears often prematurely in the placenta, as in other organs. It is natural, then, that toxic changes should influence such a physiologic change.

DR. BARTHOLOMEW (closing).—The work covered such a mass of data that it was very hard to present all the various facts in the time given but I must admit this, that in the first half of any such work when one is rather unfamiliar with the type of infarcts and has not classified them in his own mind as to etiology and types, the results will necessarily differ somewhat from those obtained in the last half of the work. We were first looking for infarcts that were definitely demarcated, and of a yellow or white color, not realizing the importance of the early infarcts that Young has so clearly described. In the last half of this work, and since the data have been collected, I believe that I cannot recall a single case of fulminant toxemia that has not shown this acute type of infarction. I believe that when the condition comes to be studied more in detail the types of infarction that I have just tried to emphasize, the acute and subacute lesions, will come to be recognized as quite a common finding in eclampsia.

As to the objection that the same lesions in experimental animals can be produced by extracts from other organs, I do not believe that is an objection. The poisons are common to any cellular tissue. We carried out the experiment of autolyzing human

liver, and obtained the same lesions in the kidneys and liver. Similar protein split products are produced, hence we obtain the same type of lesion in the liver and kidney.

While I do not, as yet, regard the work as an absolute proof that toxemia results from infarction of placenta, I do believe that it is the most fruitful and promising field for investigation and if this work will stimulate, in all clinics, the methodical examination of placentas, correlating the lesions and the symptomatology, I believe that it will be put on a firm footing.

Increase in Guanidine Compounds in Eclampsia; An Experimental Study, Dr. Paul Titus, Pittsburgh, Pa. (By Invitation.) (See page 667, November issue.)

DISCUSSION

DR. OTTO H. SCHWARZ, St. Louis, Mo.—Several years ago, Dieckmann, by injection of tissue fibrinogen intravenously and by feeding animals raw meat, was able to produce very extensive liver lesions, simulating the lesion of eclampsia, in many dogs. This work was presented before the New York Obstetrical Society.

I believe that the liver lesion in eclampsia is usually present, but it is not necessarily an accompaniment of the disease. The theory of the development of the lesion in my opinion, is as follows:

The ferments of the blood are concerned in neutralizing placental proteins as they enter the blood stream. From the intestinal tract are absorbed protein constituents more complex than amino acids in addition to amines which result from intestinal putrefaction. This absorbed protein material is not sufficiently neutralized, coagulation time of the blood is shortened in the portal system, and with the poisons that are absorbed, the endothelium can be readily damaged and coagulation with subsequent hemorrhage take place. I, therefore, think that no specific poison such as tyramine, histamine, or methyl guanidine is the toxic substance alone involved.

Methyl guanidine has been recently receiving some attention in the toxemias of pregnancy. Stander has recently reported on methyl guanidine in the blood of eclamptic patients and finds no increase. Grow and Senn did determinations of blood guanidine in some of our patients and in eclampsia they were able to confirm Standard's figures, but found guanidine markedly increased in one case of eclampsia, proven by autopsy, the patient having had no convulsions and was not in coma.

These workers also studied the blood in the early puerperium. On account of the profound changes in protein metabolism, they thought it might be of interest to study the guanidine content of the blood. Here also only normal values were obtained. To produce liver lesions similar to those in eclampsia, it seems to me that it would be rather difficult to do with substances as toxic as methyl guanidine. Some of the pictures which Dr. Titus has shown us, exhibit some damage. I would not say that the lesions are comparable with those found in eclampsia. In several of the slides, the lesions shown are not at all typical of the lesion in eclampsia.

DR. TITUS (closing).—I quite agree with Dr. Schwartz that some of the slides are not convincing, particularly because they were purposely selected to show merely the various stages in the familiar degenerative lesions of the liver as we developed them experimentally. The one showing the focal necroses is the most suggestive.

We have been strongly impressed by the similarity between the liver lesions produced artificially by Dieckmann, to which he refers, and those seen in eclampsia.

A problem which we are working on at present is an attempt to combine Dieckmann's ideas with ours by agreeing that the placenta is the reasonable source of his thromboplastin. To this end, therefore, we are now giving guanidine injections to pregnant guinea pigs because they have a placentation similar to human beings. We have already

noticed that the toxic and the lethal doses for these pregnant animals is considerably smaller than for nonpregnant ones, indicating that an increased susceptibility to this toxine is caused by pregnancy.

May I emphasize that this entire work which I have presented is still on an experimental basis.

A Type of Pelvis Intimately Associated With Occipitoposterior Position, Dr. Herbert Thoms, New Haven, Conn. (Published elsewhere.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MARCH 3, 1932

Dr. J. W. Cutler presented (by invitation) **Artificial Pneumothorax and Pregnancy With the Report of Two Cases.** (See original article, page 914.)

Dr. C. B. Lull presented **A Preliminary Report on the Use of Barbiturates With Ether by Rectum.** (See page 888 for original article.)

DISCUSSION

DR. NORRIS W. VAUX.—I can unqualifiedly say that of all the analgesics, the barbiturates with ether have, after careful observation in a short series of cases, been most gratifying and successful in our hands. However, I do not believe it wise to use this method routinely. It is not at all good in the rapid deliveries of multiparae. The outstanding facts in these cases are as follows: (1) With the Gwathmey method we formerly had to wait until the labor was well established. With barbiturate ethyl that is not necessary. It does not seem to slow up the labor, which so often happened when we gave the Gwathmey analgesia too soon after the onset of labor. (2) With the cases under consideration we have observed that there has been no trouble with the establishment of the primary respiration of the newborn; whereas with the Gwathmey method we had difficulty with this complication. The infants seem to be born with a good color and a rather husky cry, even though ether has been added for low forceps delivery.

This preparation must be given by someone who is familiar with the technic of rectal analgesia. The patients remain in a condition of semicoma, but do not become entirely anesthetized. They are not able to coordinate or cooperate with the doctor in the second stage of labor.

DR. JOHN C. HIRST.—I wish to emphasize one addition to the advantages mentioned, namely the prolonged duration of Nembutal with ether, which obviates the unpleasant necessity of repetition as often experienced with the ordinary Gwathmey method.

In addition to the characteristic dry lips and flushing of the face from barbiturates, an occasional extremely rapid pulse rate will be encountered, which in two instances in my own experience has been quite alarming. Furthermore, one further precaution should be mentioned, that is the necessity for observing these patients after the birth of the baby as well as during labor.

DR. LULL (concluding).—I have not observed any rapidity of pulse in this series of cases as we did with sodium amytal.

DR. C. H. FRAZIER AND DR. HENRY F. ULRICH presented (by invitation) a paper entitled **Pathology of the Thyroid Gland Complicating Pregnancy.** (For original article see page 870.)

DISCUSSION

DR. PHILIP F. WILLIAMS.—We probably see fewer thyroid cases in this area than may be seen where endemic goiter is prevalent. But only about ½ of 1 per cent of these patients show symptoms of thyrotoxicosis during pregnancy.

I do not coincide entirely with the idea that pregnant women need iodine routinely as a part of prenatal care. I doubt very much if any of us feel that 10 per cent of our prenatal cases show sufficient hyperthyroidism to need this.

The more marked cases of hyperthyroidism stress the point which Dr. Frazier has brought up, i. e., that marked dysfunction of the thyroid gland is really no part of the pregnancy, it is a complication of pregnancy and should be handled by a thyroid surgeon. Basal metabolism alone may be misleading; it is the whole group of symptoms that must lead us to determine whether thyroidectomy is necessary. Any woman who shows severe symptoms should be seen by a thyroid specialist. Not all cases will have to have the gland removed. Probably not all cases will go through pregnancy, but certainly very few will have to have the pregnancy interrupted.

I have had three recent cases with marked thyroid disturbance. The first was a primipara, aged forty-four. She was anxious to have the child, having been sterile for a number of years. Her amenorrhea was thought to be due to a natural menopause but she was four months pregnant when I first saw her. She had a basal metabolism rate of seventy plus and a pulse rate of 144. With rest in bed and mild sedative treatment, but no iodine, she quieted down. Thyroidectomy was not considered for fear of a miscarriage, she went to term, had a ten-pound female child delivered by cesarean section on account of a breech presentation, and stood the anesthesia well, in spite of the thyroid condition. The symptoms became worse after the pregnancy and two years after the delivery a thyroidectomy was performed.

A second case, also a primipara, was one of marked exophthalmic goiter complicating pregnancy at term, she had had no rest, no treatment, no iodine during the pregnancy, and went through a normal labor. An operation was suggested but it was refused and she left the hospital in poor condition.

The third case had symptoms of a severe thyrotoxicosis. She received iodine 3 or 4 times during the five months of pregnancy during which she was observed, went through a normal labor, and showed marked improvement after delivery.

Two other cases were those of women upon whom thyroidectomy had been done. One went through 2 pregnancies without any disturbances and the other through one.

DR. EDWARD ROSE.—Several questions seem to me to be deserving of special mention:

1. The importance of the administration of iodine to pregnant women with and without goiter. An insufficiency of iodine may and often does result in the appearance of goiter and cretinism in the infant, even though the mother has had no apparent abnormality of the thyroid gland. This constitutes more of a problem in endemic goiter districts than in our own region. But it is a very simple and easy matter to assure the pregnant woman of an adequate supply of iodine simply by administering 10 mg., either in liquid or tablet form every week or two throughout her pregnancy. And since 50 mg. of iodine is sufficient to enable the adult thyroid gland to carry out its function during a year under normal circumstances one can easily make sure that both mother and infant have a good supply.

I believe that the routine administration of iodine to pregnant women is just as important a part of prenatal care as any other, and should be a part of all prenatal routine.

In cases where there may exist a simple, nontoxic, diffuse goiter, the dosage of iodine and the frequency of its administration should be increased somewhat. And even in the presence of hard or nodular nontoxic goiter, it is safe to administer iodine if it is done cautiously and the patient is kept under strict and frequent observation.

2. The tendency of pregnancy to be followed by an aggravation of preexistent simple goiter, or hyperthyroidism, or by the development of simple or toxic goiter is well known. In 635 cases at the University Hospital which Dr. Frazier and I analyzed in 1930, 9.9 per cent of the women with toxic goiter, stated that pregnancy immediately preceded the onset of their symptoms, or greatly increased them. I know that there is considerable difference of opinion on this subject, but I feel that pregnancy is a very important etiologic factor in both hyperthyroidism and simple goiter.

I am glad that the speakers refrained from assuming a dogmatic position on the necessity for or value of thyroidectomy in these cases. Here again there is a very great variety of opinion. It is generally true that most pregnant patients stand thyroidectomy very well, but any operation presents a threat to the continuation of pregnancy which cannot be ignored. I feel that discretion should be used in these cases and that a trial with iodine is often worth while. Even though the patient cannot be cured, she can often be carried along in a reduced state of toxicity and have the operation performed after labor.

DR. EDWARD A. SCHUMANN.—Until a short time ago surgeons have been reluctant to operate upon patients presenting evidences of acute thyroid toxemia during pregnancy.

There is one point to which I beg to direct attention, the occasional occurrence of rapidly developing symptoms of thyroid toxemia during pregnancy, which symptoms, whether treated or not, last perhaps a month or six weeks and then gradually decline in severity, disappearing after delivery. Patients suffering from this syndrome might readily be subjected to unnecessary thyroidectomy.

DR. FRAZIER (closing).—In the discussion on the relation of thyrotoxicosis to pregnancy one question has not been touched. For how long after an operation for the relief of thyrotoxicosis should the patient be cautioned against conception. In the patient already married or in the one contemplating matrimony our opinion is frequently sought and invariably we recommend an interval of at least a year. In those cases operated upon in the pregnant state we recommend an interval of two years.

In certain of the severe cases in our series that were operated upon during pregnancy, the induction of labor had been seriously considered. I do not believe that this should ever be considered as an appropriate way of managing a toxic thyroid during pregnancy or to put it another way, the principles underlying the treatment of toxic goiter during pregnancy differ in no respect from those in the nonpregnant state. Once the diagnosis is established it is safer for both mother and child to remove the toxic gland.

DR. B. C. HIRST AND DR. I. ANDRUSSIER presented a paper entitled **Uncomplicated Prolapse of the Ovary, Due to Elongation of the Infundibulopelvic Ligament, Its Treatment.** (For original article see page 879.)

DISCUSSION

DR. EDWARD A. SCHUMANN.—Penrose, Baldy and Beyea laid great stress upon this condition, regarding it as frequently congenital in origin, though often due to subinvolution of the uterus following pregnancy or abortion. The left ovary

seems to be more frequently affected than the right and a characteristic symptom is pain on defecation.

DR. G. M. LAWS read a paper entitled **Results of Operations for Prolapse of the Uterus and Bladder.** (For original article see page 864.) This was briefly discussed by Drs. J. H. Girvin and S. E. Tracy.

NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 9, 1932

DR. CARL H. ILL, of Newark, N. J., presented (by invitation) **Two Cases of Pregnancy Following Watkins' Interposition Operation.**

Mrs. D., aged thirty-seven, was operated upon May 25, 1930, for a relaxed perineum, marked cystocele, and lacerated cervix. The cervix was amputated, and a typical Watkins' interposition operation done. Both tubes were doubly ligated, with linen thread, severed with cautery between the two ligations and stumps buried in the folds of the broad ligament. She also had a perineorrhaphy. She menstruated last on June 4, 1930, and was referred to me for delivery on January 4, 1931.

She had had three children; the first a long difficult labor, terminated by forceps.

She was never well after this, having painful menstruation headaches, backaches, and a feeling of everything dropping out of her vagina. These symptoms practically cleared up while she carried the other children. She felt well during this entire pregnancy, her only complaint being frequency of urination and burning at times. Examination when she came to me showed head high, but engaged in the pelvis, a long anterior vaginal wall, the scar of the interposition operation was very definitely felt. Blood pressure normal, urine negative except quite a few white cells.

On February 18 she came into the Hospital with slight pains. Abdominal examination showed back to the left, feet distinctly felt to the right; fetal heart rate 120, left lower quadrant. Pelvic examination showed head in midpelvis, pointing toward the rectum, anterior lip of cervix 10 cm. long. Diagnosis of left occiput posterior. Her pains soon stopped; castor oil and quinine were given the night of the twentieth followed by six 3 minim doses of pituitrin. At 10 A. M. on the twenty-first, vaginal examination showed head still in midpelvis, anterior lip of cervix 5 cm. long; cervix 5 fingers dilated. A sound was passed into the bladder, after catheterization, and was easily inserted for 6 inches. In fear of injury it was not passed any further, no obstruction being encountered. Caput was visible on February 22 at 4 A. M.; living child was easily delivered with low forceps in R.O.A. position.

After waiting one hour placenta was delivered manually. It was not thought advisable to use much force by Credé's method.

She reported on April 7 for follow-up. Perineum was somewhat relaxed, vagina subinvoluted, and a slight erosion of the end of the cervix. Uterus small, antiverted, no cystocele. She is now entirely well and has no pain at menstruation.

The second case, Mrs. S., aged twenty-nine, was referred to me September 4, 1931. She had had two children; the first after one hour's labor and the second after two pains. Both babies were said to have weighed over 10 pounds. In March, 1927, she was operated upon for a marked cystocele, rectocele, and lacerated cervix. The cervix was amputated, typical Watkins' interposition operation done, both tubes being doubly ligated with linen thread, severed with cautery between the ligation, and ends buried in the folds of the broad ligaments.

She menstruated last on February 15, 1931. Abdominal examination showed a hard, firm uterus, which was very definitely held down over the bladder region. Vaginal examination showed a very much elongated and thickened wall of the vagina, and the cervix was so far posterior that it could hardly be felt. She was very uncomfortable, had great difficulty in urination and had to be in bed most of the time. Her blood pressure was normal, urine showed considerable albumin, and 4+ pus. Her condition grew steadily worse, urinary symptoms increased, she had severe pains all through her abdomen. On October 19, 1931, a typical classical cesarean section was one, a living male child being delivered. On opening the abdomen the bladder was pulled way down under the pubes, and when the uterus was opened the anterior wall was 7 cm. thick. The posterior wall was extremely thin. The entire uterus had developed posteriorly, just as it so often does in a pregnancy following a ventral fixation. No opening into the uterus could be detected where the tubes had been cut. However, the location at both horns of the uterus were sewed over by redundant peritoneum.

She made an uneventful recovery and on her follow-up examination on January 4, 1932, showed perineum and cervix normal, uterus anteverted, small, no cystocele. Abdominal scar healed; patient has no discomfort.

In the first case the uterus developed normally and pulled the bladder up with it. Consequently, there was no obstruction and the baby was born normally. In the second case the uterus entirely developed posteriorly, causing a thick anterior portion, which almost entirely obstructed the birth canal, acting exactly like a fibroma which had developed in the lower anterior segment.

DR. O. PAUL HUMPSTONE.—I have observed two patients who became pregnant after the Watkins' interposition operation. The most important point in these cases is whether or not the cervix is amputated. If the cervix is amputated in the interposition operation, the os will not dilate in labor.

DR. HARBECK HALSTEAD.—I have seen only one of these cases and we did a low-flap cesarean section because it was not possible to do anything else.

DR. ROBERT T. FRANK.—The thing that strikes me most is the question of the technic in sterilizing these patients at the time. In my own experience, which covers quite a large series of cases, probably over 500, I have noted only one pregnancy after ligation of the tubes. I lay great stress upon not peritonealizing these two transected ends in tying them with a single ligature, tying over the loop, first to one side and then to the other. I transect them with the scissors and take great care to see that the openings are parallel to each other and not peritonealized, because should reestablishment of the lumen occur the likelihood of the ovum finding the second entrance is much reduced. On the contrary, if a normal tube, just like a normal vas deferens, is buried after transection in a connective tissue sheath, the likelihood of reestablishment of continuity is greatly increased.

DR. ELIOT BISHOP.—The only thing I want to emphasize, as I have many times before, is that the actual sterilization is done by peritonealization, and not by artificial blocking. We have had no pregnancies follow this theory and practice of sterilization. About three years ago we collected over 100 cases and have had a number of additional cases since then. We cut off a loop of each tube over catgut ligature and leave the two ends parallel, as Dr. Frank mentioned. The ends slowly pull apart after peritonealization, which occurs in twenty-four to forty-eight hours. We have had the opportunity of opening two or three abdomens and have been able to demonstrate this.

DR. ALFRED C. BECK.—I recall some years ago treating a pregnant woman who had had an interposition operation and amputation of the cervix by Dr. Polak.

I do not recall whether he sterilized her or not; probably he did tie off the tubes. In that case I pulled a foot through the cervix, although it was very difficult to reach. Finally, the cervix dilated and a living child was delivered spontaneously by the breech.

DR. RALPH M. BEACH.—I would like to report a case of interposition during the childbearing period by Dr. Polak at the Jewish Hospital. At about the third or fourth month this woman developed a very marked elevation of the bladder, elongation of the urethra, marked clouding of the urine, distortion of the ureters, bilateral hydronephrosis, which was followed by retention, very marked toxemia, and jaundice. When she was brought to the hospital she was very sick. We emptied the uterus at this time, very easily, by an anterior hysterotomy. There being no bladder in front of the uterus, it was a very simple procedure. Following that the patient made a very rapid recovery.

DR. RALPH A. HURD.—Sterilization of women in the childbearing period when an interposition operation is done, should always be preceded by curetting. In my case the patient menstruated about the middle of May and I operated upon her in the Woman's Hospital the first week in June. I took great care to insure her against future pregnancies, but rather inadvertently neglected to curet the uterus. It seemed that she was pregnant at that time; she became pregnant between her last menstruation and her admission to the hospital, and she went on almost to term. I suspected a low implantation of the placenta, although I was never able to prove it on account of the great difficulty of examination. I did a cesarean section and she had a live baby five weeks from term. I think the sterilization has been well done because she has not become pregnant again.

The tubes were apparently occluded completely and the two cut ends were separated and closed, or peritonealized thoroughly. I had to make the incision way up on the fundus, practically on the posterior wall of the uterus. The bladder was drawn up to the top.

DR. BENJAMIN P. WATSON.—I believe that all of these complications could have been avoided had interposition not been done. I regard it as a bad operation.

DR. CARL H. ILL.—I did not operate originally on either one of these cases. They were referred to me for care during pregnancy. Both patients were Catholics, they would not consent to interruption of pregnancy, there was nothing else to do and, so, I had to let them go through with it. It so happened that both these cases were done by Edward Ill, and in going over his records with him I found that he has done almost 600 interposition operations. He has a very careful follow-up system and these are the only cases that he had that have ever become pregnant. He has used this method of sterilization, he tells me, for the last twenty years.

DR. JOHN J. MADDEN (by invitation) read a paper entitled **The Rôle of Calcium and Viosterol in Pregnancy.**

DR. VICTOR JOHN HARDING AND DR. H. B. VAN WYCK, of Toronto, Ont., (by invitation) presented a paper entitled **Researches on the Toxemias of Later Pregnancy.** (For original article see page 820.)

DISCUSSION

DR. H. B. VAN WYCK.—One of the striking things about the toxemias of pregnancy has always seemed to me to be the extreme number of varying types with a certain common association, and I feel that that has been too little taken account of in all etiologic discussions. We see that factor, too, in the difficulty that has been

encountered in arriving at any satisfactory method of classification. This so-called classification, you would say, looks worse than ever; but it is no classification at all. It relieves us of the necessity of giving a name which immediately becomes a bone of contention in these variable conditions, and it focuses our attention on the actual tissue and chemical changes which we see in any individual case. I think that is a valuable point of view, as well as Dr. Harding's suggestion that the formation of some of these as yet unknown combinations may be a starting point for further investigation.

With regard to the dietetic factor, the second part of the paper, may I say that the results of these experiments show that the only dietetic factor is salt.

The third part of the paper is in harmony with the hypothesis of salt and water disturbance, inasmuch as it seems to explain the success that has met with so many apparently, at first, discordant methods of treatment. With all these treatments, based on a variety of ideas, there is a certain proportion of success to be met with, and this is further in support of the hypothesis. After all, in these conditions in which prophylaxis is of peculiar importance and is in all our hands of peculiar efficacy, the test of any hypothesis to explain these conditions will be, I think, borne out chiefly in the extent to which it places in our hands a prophylactic agent, and I can, speaking from experience assert that this hypothesis is of value. In the last five hundred obstetric patients I have kept careful weight records. I expect that they shall gain three or four pounds a month or less. When they exceed that limit I then consider it necessary to take further steps. This simply is closer prenatal supervision, rest, and salt restriction. I know the fallacy of attempting to estimate any prophylactic success from anybody's series or any number of cases. The only fact that I can state in this 500 is that out of that number there were no serious toxemias and only three in which hospitalization was necessary. It is rational, at any rate, and would seem to be in harmony with the hypothesis.

DR. W. W. HERRICK.—Dr. Harding's opinions about the nature of the late toxemias of pregnancy are very much in accord with my own. The abandonment of the attempt to find a single cause and the attempt to correlate these disturbances with general medical conditions, has for many years seemed to be most desirable.

Recognition that the liver, the kidney, the cardiovascular system, and the nervous system bear the brunt of the late toxemias of pregnancy and that the clinical study of these patients often brings to light underlying defects in these important organs is a point of view which the obstetrician is rapidly accepting.

We recognize latent or obvious nephritis and hypertensive cardiovascular disease as being very definitely related to these toxemias. Hepatic disability is less well defined. Its rôle awaits the development of satisfactory tests of hepatic function.

One point deserves special emphasis. The internist believes that he can differentiate chronic nephritis and essential hypertension or hypertensive cardiovascular disease. In obstetric circles there is still a tendency to consider these two conditions as one. Careful follow-up studies and the observation of the behavior of patients with essential hypertension in pregnancy reveals the great importance of cardiovascular disease as distinct from nephritis in the late toxemias of pregnancy.

I believe the etiology of these toxemias will be found in many instances bound up with that of hypertensive cardiovascular disease as at present recognized by the internist. The solution of this problem awaits added knowledge in physiology. Dr. Harding's studies are an important step in this direction.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF APRIL 1, 1932

DR. GEORGE G. COCHRAN, JR., presented a paper on **Avertin Analgesia in Obstetrics.** (For original article see page 849.)

DISCUSSION

DR. JOHN CASAGRANDE.—I have followed a number of cases under avertin analgesia, and have used it in five cesarean sections. I have used 80 mg. instead of 60, supplemented by gas and oxygen. In cesarean section the patients come out of the anesthetic in two or three hours after the operation, free from nausea or vomiting, and they certainly seem to recover a little better than they do with ether or other general anesthetics.

DR. COCHRAN.—The greatest number of doses I have given any one patient is three, and that was in a forty-eight-hour labor.

We have observed no excessive bleeding after cesarean section in which avertin has been used.

DR. BARTON C. HIRST read a paper entitled **Some Experiences in the Diagnosis and Treatment of Congenital Anomalies of the Female Genital Tract.** (For original article see page 843.)

DISCUSSION

DR. ISIDOR C. RUBIN.—I believe the question of the formation of an artificial vagina resolves itself into a decision between two technics. One consists in utilizing the labia minora. I have had one experience with this which was most gratifying. The patient remained at the hospital seventeen days. I had an opportunity to examine the patient several years after operation and subsequent to marriage, and she had been having perfectly satisfactory coitus. Another procedure is the one devised by Frank and Geist. The end-result after their operation is most satisfactory and permanent. It requires considerable patience in planning the plastic and in carrying out the technic later. However, it requires a minimum of six weeks of hospitalization and longer in some cases.

Urethral coitus, which is occasionally encountered, appears to be satisfactory to such couples. The combination of anomalous conditions in the genital or urogenital sphere and remote organic anomalies is also well known.

DR. G. W. KOSMAK.—The field of genital deformities in the female is one of intense technical interest, and yet, it may be advisable in many cases to let well enough alone, because even the successful technical accomplishment of the restoration of the vaginal canal, so-called, may lead to a considerable degree of trouble later on. I doubt whether the restoration of an anatomic result is sufficient in most cases to make up for the lack of physiologic background, and I believe that is one point which many of our expert plastic operators have missed. While they may be able to restore anatomic details, they are not able to develop the physiologic background which is necessary in a case of that kind.

DR. ERNEST D. RESNIK.—I would like to report a case of a patient twenty-two years old, who gave a history of amenorrhea of ten weeks' duration. She was admitted to the hospital with a diagnosis of incomplete abortion. Examination rectally showed an apparently normal uterus on the right side, and on further examination a large mass was found on the left side, the size of a four and a half months' pregnancy. Further inspection revealed a complete duplication of the uterus cervix and vagina. On speculum examination the right small uterus had a small piece of placenta protruding through the cervix indicating a pregnancy and abortion on the right side, and the uterus on the left side was still carrying the pregnancy at about four and a half months.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Abortion

Grann-Petersen: Treatment of Abortion. Ugesk. f. laeger 92: 837, 1930.

This report is based on 1118 actively treated cases of abortion out of 1146 hospitalized cases. The gross mortality was 0.61 per cent while that of the actively treated cases was 0.45 per cent. The afebrile cases numbered 747 and these were treated without mortality while in 371 febrile cases the mortality was 1.35 per cent. The incidence of genital complications following operation was 1.21 per cent in the afebrile and 3.5 per cent in the febrile cases.

After a review of these cases and some of the current literature on the subject the author concludes that the *one* indication for operative treatment (curettage) is an abortion which is already under way but that such conditions as ectopic gestation, induced abortion, complete abortion, salpingitis, parametritis and peritonitis must first be ruled out. Hemorrhage and infection are usually best avoided by early emptying of the uterus whether the case is febrile or not. In the later months of pregnancy, expectancy may be practiced and, in the presence of genital complications, interference is contraindicated. The treatment must be individualized as no rules will fit all cases.

The author subscribes to the following indications for emptying of the uterus as promulgated by Prof. Leopold Meyer: a widely dilated cervix through which the gestation products are easily passed; strong hemorrhage or exsanguination from a previous hemorrhage; and a febrile postabortal convalescence or foul smelling postabortal discharge.

REUBEN L. LARSEN.

Reichelt, H.: The Treatment of Abortion During the Last Ten Years. Monatschr. f. Geburtsh. u. Gynäk. 84: 357, 1930.

From 1919 to 1929, there were 1,870 cases of abortion at the Breslau Woman's clinic. The treatment of these cases was neither entirely active, nor entirely expectant. The usual treatment was that of "the middle line therapy." In cases where no fever was present, cervix patulous and adnexa normal, an immediate curettement was performed. If the cervix was closed, quinine was administered. Of the 674 afebrile cases 85.6 per cent were discharged cured, 14.3 per cent left the hospital improved and 0.1 per cent died. In 1,196 cases fever was present. Of these 82.2 per cent were treated actively, 6.9 per cent expectantly and 10.9 per cent conservatively. Among the 1,196 cases, 74.1 per cent were cured, 22.1 per cent were improved and 3.8 per cent died. Of all the 1,870 cases, 82.5 per cent were cured, 14.3 per cent were improved and 3.2 per cent died. The chief causes of death in the 60 fatal cases were sepsis (19), peritonitis (11), grippe (6), embolus (5), poisoning (4), purulent endometritis (4) and pneumonia (3).

Twice as many unmarried girls have abortions as married women and in contrast to the latter, the number of abortions decreases among the unmarried girls as their

age increases. In the entire series of cases, 5.9 per cent were therapeutic abortions, 11.3 per cent had definite causes, 10.7 per cent were distinctly criminal and 72 per cent were presumably criminal. J. P. GREENHILL.

Olow, J.: Some Views on the Treatment of Miscarriages. Acta obst. et gynec. Scandinav. **9**: 399, 1930.

The author favors active treatment of abortions for febrile as well as afebrile cases. In his series of 740 cases 300 had fever. The only exceptions to active therapy are ectopic pregnancy, imminent abortion, completed abortion, and the presence of salpingitis, parametritis and peritonitis. The treatment was entirely expectant in 107 cases, immediate operation in 351 and operation after expectancy in 282. There were 3 deaths in the series, one due to embolus and two to peritonitis. All were subjected to expectant treatment. The morbidity was very low.

J. P. GREENHILL.

Nahmmacher: Charcoal in Abortions. Therap. d. Gegenw. **10**: 452, 1930.

The intrauterine use of charcoal is of marked value as a prophylactic measure in afebrile abortion and as a therapeutic agent in febrile abortion. The method is free from danger, simple to carry out and most rapid in its action. It is therefore a procedure which is available and practical for the general practitioner. The use of charcoal is indicated in afebrile abortion, febrile abortion, puerperal endometritis and cesarean section when done after the rupture of the membranes.

The technic of the introduction of the charcoal is very simple. The vagina is irrigated, the cervix grasped and two to four pencil shaped pieces of charcoal are introduced directly into the uterine cavity. The author does not believe in the mechanical dilatation of the cervix but always awaits spontaneous dilatation. Immediately upon the introduction of the charcoal a crackling sound is heard followed by the appearance of the foam. The cervical canal is then lightly packed with iodoform gauze for two to three hours. After that the charcoal is no longer active.

The author has treated 152 cases of abortion without charcoal and 122 with charcoal. His results in the charcoal series were markedly better both with febrile and afebrile cases. He was also able to improve his results in puerperal endometritis by the use of charcoal, especially in those patients in whom a cesarean section had been done after rupture of the membranes. RALPH A. REIS.

Otto, Karl: Experiences With the Non-Operative Termination of Pregnancy by Means of "Interruptin." Zentralbl. für Gynäk. **56**: 112, 1932.

"Interruptin" is a mixture of iodine and thymol in a fatty base. The author reports its use in twenty-four cases of pregnancy between 2 and 5 lunar months over a period of one year. Complete emptying of the uterus occurred at the conclusion of pains in only 4 cases, and in 2 cases there was bleeding of between 700 to 800 c.c. Twenty-three of the cases were afebrile during the puerperal course, and the other case ran only a slight temperature. Operative removal of part of the uterine contents by curettage was necessary in 15 cases. WILLIAM F. MENGERT.

Engelmann, F.: The Danger of "Interruptin." Zentralbl. für Gynäk. **56**: 119, 1932.

The author has collected from literature about 250 cases in which "Interruptin" has been used to terminate pregnancy and in that number has found 5 fatalities. Three of these were due to emboli, either fat or air, and the cause of the other two deaths was not ascertained. WILLIAM F. MENGERT.

Lindqvist, E.: The Abortions in Malmo, 1897-1928. Acta obst. et gynec. Scandinav. 12: 306, 1932.

The case histories of 2,235 cases of abortion and more than 25,000 deliveries at the Malmo General Hospital from 1897 to 1928, inclusive, have been carefully studied by Lindqvist with regard to a number of different conditions, and subjected to statistic compilation and investigation.

The number of living children born to each 1,000 women between the ages of 17 and 45 has decreased in Malmo, the legitimate births falling from 245 in 1908 to 90 in 1927, and the illegitimate ones from 52 in 1908 to 19 in 1927.

The number of abortions registered annually in Malmo has risen from 121 in 1910 to 282 in 1927.

A previous pregnancy or abortion does not in itself appear to create any predisposition to genuinely spontaneous miscarriage in a later pregnancy.

A study of the frequency of abortion in different groups of married and unmarried women, especially as compared with the frequency of abortion in married primiparas suggests that there is extensive criminal abortion in all the groups except that of married primiparas.

The following approximate percentages of the total miscarriages in the last few years were due to criminal abortion: 10 per cent in married primiparas, 50 per cent in married secundiparas, 80 to 90 per cent in married tertiparas and multiparas and in unmarried women.

The percentage of repeated abortion rapidly increases in proportion to the number of previous pregnancies; among sextiparas, 48 per cent had aborted before, and of these 18 per cent had done so more than once.

Genuine spontaneous abortion probably appears more commonly after the end of the third month of pregnancy than earlier.

Unmarried women have apparently been practicing criminal abortion at an earlier stage of pregnancy the last few years than previously.

The frequency of febrile abortions was about 21 per cent in married women, and about 26 per cent in unmarried ones.

Of the total number of abortions at the hospital, 1.2 per cent terminated in death. Most of the deaths occurring among patients with septic abortion were probably due to criminal measures.

The mortality from abortion was as follows: For the afebrile cases 0 per cent. For the febrile cases with a rectal temperature between 38° and 38.5° C., 2.3 to 5.9 per cent and for the febrile cases with a rectal temperature of 38.5° C., or more, 5 to 13 per cent.

J. P. GREENHILL.

Erratum

In the discussion by Dr. Arthur H. Curtis on Dr. W. T. Dannreuther's paper, page 781 of the November issue, an error has occurred in the third line of the first paragraph. The latter should read as follows: "Consideration must be given to the age which a patient shall have attained before she is a fit subject for radium treatment of a nonmalignant condition" not a malignant condition.

INDEX TO VOLUME XXIV

AUTHORS INDEX*

*July, pp. 1-158; August, pp. 159-318; September, pp. 319-480; October, pp. 481-634; November, pp. 635-796; December, pp. 797-950.

SUBJECT INDEX*

*July, pp. 1-158; August, pp. 159-318; September, pp. 319-480; October, pp. 481-634; November, pp. 635-796; December, pp. 797-950.

C

D

E

F

H

P

U

V